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DIVERTICULA OF THE DUODENUM

NATHAN S. DAVIS, III.

(From the Pathological Laboratory of Rush Medical College.)

Diverticula of the alimentary canal are not uncommon. According to a recent and comprehensive article by Buschi,[1] they are most common in the colon, next in the ileum, then in the esophagus, pharynx, duodenum and stomach in the order mentioned. Some writers believe that diverticula of the duodenum are as common as Meckel's diverticula of the ileum; others that they constitute 11 per cent. of all varieties of diverticula of the alimentary canal. The retroperitoneal location of most of these, without doubt, is in some measure responsible for the failure of duodenal diverticula to occupy any rôle in clinical affairs. Found about twice as frequently in the bodies of men as in those of women and with an increasing frequency in those of older persons, 16 per cent. below 50, 37 per cent. between 50 and 60, 47 per cent. over 60 years, these diverticula in practically all instances have been first met with in post-mortem examinations.

Since the diverticula of the duodenum I have examined are all in the descending or transverse portions of this part of the bowel, I will consider only similar diverticula and will not include dilatation of the biliary and pancreatic ducts.

In size they are from 1 to 5 cm. in their greatest dimensions; they are frequently referred to as hazel-nut size or even as large as hen's eggs. They are located along the line of mesenteric attachment near the ampulla of Vater and are called by the French "diverticules

1. Virchows Archiv., 1911 (206), 121.

perivateries." Of the sixty-four cases reviewed by Buschi,[1] there were fifty-four he thought well authenticated. Since his contribution, Bauer[2] has reported two more and the five I have examined make the whole number sixty-one.

As has been the case with others who have examined these anomalies, those I have studied were obtained postmortem; for one of them, found in the dissecting room,[3] I am pleased to thank Dr. Harvey.

1. Ten centimeters distal to the pylorus and 3 cm. to the right and 2 cm. distal to the ampulla of Vater, there is an oval opening 2 by 1.6 cm. leading into a diverticulum, the greatest dimensions of which are 2.8 by 2 cm. The walls of the pouch are quite thick but do not appear to contain any muscle; however, there is a distinct ridge of muscle about the opening. By transillumination a blood-vessel is seen joining and entering the diverticulum at its most distal point with smaller vessels leading from it.

2. One centimeter distal to the ampulla of Vater, there is an opening 3 by 5 cm. in its greatest dimensions which opens into a diverticulum 8 by 10 mm. As in the first described, the blood-vessels radiate from the end of the pouch.

3. Two centimeters distal to the ampulla of Vater, there is an opening 1 by 0.5 cm. into a pouch 3.6 by 2.2 cm. The wall of this diverticulum is very thin and the arrangement of the vessels is the same as in the others.

4. Three centimeters distal and 0.5 cm. to the right of the ampulla of Vater there is an opening 0.7 by 0.5 cm. into a diverticulum 3 by 2 cm. in its greatest diameter. It has no muscular coat and the arrangement of the blood-vessels radiating from its tip is similar to that already mentioned.

5. Seven-tenths centimeter proximal to the ampulla of Vater there is an opening 0.3 cm. in diameter into a diverticulum 2 by 0.5 cm. and similar in all respects to the third of these. There is also a second opening

2. Wien. klin. Wchnschr., 1912 (25), 879.
3. Anatomical Department, University of Chicago.

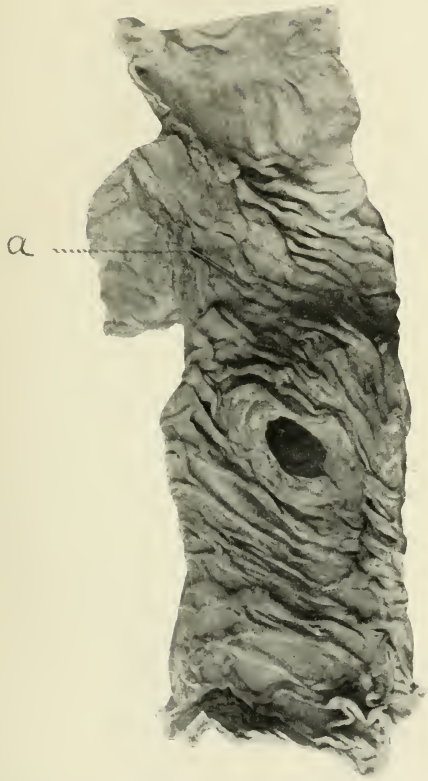

Fig. 1.—Diverticulum of the dudodenum viewed from the interior of the bowel. a, Orifice of the common bile duct.

3 mm. distal to the ampulla of Vater, 4 mm. in diameter and leading into another diverticulum 2.3 by 0.7 cm. From the superior wall of this, there is a slight secondary out-pouching 1 by 0.3 cm. in its greatest dimensions. Both of these pouches are also quite like the third described. As the vessels had been injected in this fifth example the location in these two pouches where an artery pierces the muscularis is more easily seen.

As has been stated, there are no gross indications of any muscular coat in these diverticula. Buschi[1] claims to have found atrophic fibers in some but most observers have found the muscular coat absent. The mucosa is said to be unchanged except that Brunner's glands are absent; the muscularis thickened, the serosa unaltered; some proliferation of connective tissue between the serosa and mucosa is described.

The diverticula reported by Bauer[2] are similar to those I studied and also to those forming the basis of Buschi's[1] article. In no instance have changes in the liver, pancreas, bile- or pancreatic-ducts been observed. The lining of these diverticula is subject to the same changes as the duodenum. I have found only one instance in which there have been symptoms for which a diverticulum of the duodenum may have been responsible and here, too, the diverticulum was not found until after death. The symptoms were those of a dilated stomach and obstruction, vomiting, loss of weight, cachexia, etc., for which a gastro-enterostomy was performed, although at the operation no lesion was found to account for the symptoms. A few days later the patient died of a bronchopneumonia. The diverticulum was 3 by 5 cm., filled with a thick chylous fluid and Bauer[2] believed that the traction it exerted was sufficient to cause the obstruction. A second cherry-sized diverticulum was also present.

Diverticula of the alimentary tract are generally referred to as either true and congenital or false and acquired. The characteristics of true diverticula are that all layers of the intestine, the mucosa, muscularis and serosa must be present in their walls. Although

Fig. 2.—The same diverticulum illustrated by Figure 1, seen from in front. a, The head of the pancreas.

Bauer,[2] Buschi, Volker[4] and Seippel,[4] who have found atrophic muscle fibers in some cases, believe that these diverticula are true and congenital there are some reasons why the view of Klebs[5] that all the diverticula of the intestines in which the musular coat is absent are formed as herniations of the mucosa through the muscularis, should apply equally well to these duodenal pouches. These herniations, he believes, are produced by traction of the blood-vessels which, piercing the muscularis, are very intimately connected to the mucosa. After traction has formed a ring-shaped protrusion, the pouch enlarges along the path of least resistance which is not necessarily the sheath of the blood-vessels but may be any part of the mesentery, and this latter increase in size may be due largely to increased pressure within the bowel. Hansemann[6] demonstrated that the weakest point in the intestinal wall is at the entrance of the blood vessels by ligating segments of bowel, filling them with water and thus increasing the pressure in them when hernias formed where the blood-vessels met the exterior of the bowel.

To support his view of the congenital origin of these diverticula of the duodenum, Buschi[1] states that there are muscular fibers present and hence they are true diverticula. He admits, however, that these fibers are atrophic. Opposing are the facts that a few fibers might readily be drawn through with the hernias of the mucosa, and that the muscle fibers in other diverticula such as Meckel's, a true congenital diverticulum, undergo no marked atrophy in postnatal life.

Furthermore it is alleged that the occurrence of diverticula of the duodenum in children dying of congenital stenosis of this part of the bowel indicates that they are true and congenital; but such children are extremely cachectic and in fact usually die of starvation. They also have a dilated stomach and duodenum above the point of obstruction, so there are present the chief causes for the formation of diverticula, according to the explanations of Klebs and Hansemann, i. e., marasmus and

4. Cited by Buschi, l. c.
5. Cited by Fischer, Jour. Exp. Med., 1901 (5), 333.
6. Virchows Archiv., 1896 (144), 400.

increased intra-intestinal pressure. That 84 per cent. of diverticula have been found in individuals over 50 years old, is much more significant than the presence of a few in infants dying from congenital stenosis of the duodenum.

It has been suggested that because the duodenum is the most twisted part of the alimentary canal during fetal life the diverticula there are congenital. Epithelial outgrowths in this part of the primitive foregut give rise to the liver and pancreas and their ducts. Diverticula developing during early fetal life would probably be associated with changes in the liver, pancreas or their ducts and such anomalies are rarely reported. The close apposition of the diverticula to the head of the pancreas is readily accounted for by the fact that they are formed by traction of the superior and inferior pancreaticoduodenal arteries. The absence of ulcers, tumors, stones, round worms and fecal concretions are not worth considering in this connection. Buschi states that the appendices pyloricae are of the same character, but they are not similar to what I have described.

In conclusion, therefore, the chief points in favor of diverticula of the duodenum being false and acquired are their anatomic relations to the blood-vessels; the absence of a well-developed muscular coat; the character of their mucosa; the lack of changes in the liver, pancreas, etc.; their occurrence in individuals past middle life; and, as will be seen from this table of the causes of death, their occurrence in cachectic individuals.

Causes of death:

Intestinal obstruction and broncho-pneumonia	1
Apoplexy	1
Skull fractures	1
Amyloidosis	1
Carcinoma	1
Tuberculosis	1
Nephritis	1
Chronic heart lesion	4
Senility	17
Unknown	33

October 14, 1912.

AN EPIDEMIC OF BACILLARY DYSENTERY IN INSTITUTIONAL CHILDREN

ALBERT HOWARD BAUGHER AND ROBERT J. GAY
(From the Laboratory of St. Luke's Hospital.)

The purpose of the following paper is to give a brief account of an epidemic of bacillary dysentery which occurred at the Chicago Orphan Asylum during the month of June this year (1912). In all thirty-seven children, three care-takers and a laundress were stricken. All were subject to the same source of infection, which was a child admitted to the quarantine ward of the home May 18. This fact was not learned, however, until the epidemic to be described had completely subsided. It was then found that this child had had an attack of dysentery with bloody, mucus stools six weeks prior to entrance to the quarantine ward; but which undoubtedly was in a quiescent state as all the children are watched closely in regard to the number of bowel movements. On June 3, two weeks and three days after the child had been admitted, the child vomited and began to have frequent stools. The following day a rash was noticed which proved to be measles. The stools soon became bloody with much mucus and very frequent. Before death there was almost constant evacuation. Horse serum was administered for the hemorrhage from the bowel, which apparently was effective temporarily. The temperature during the first ten days of the disease ranged between 103 and 105 F. Later it was as high as 106 F. The patient died with bronchopneumonia and exhaustion on the seventh day after the onset of the disease.

At first it was thought that the source of infection originated in the home because of the fact that most of the cases took sick at about the same time, including the case mentioned above. Therefore, the following possible sources of infection were investigated. Most of the milk used came in bulk, but it was observed that only comparatively few of the children using it contracted the disease; moreover, the dysentery occurred

only with certain groups of children; also, one baby contracted the disease that had only been fed certified milk from a well-known dairy. This evidence seems to show that the milk was not the source of infection. The water was examined by a down-town laboratory and pronounced safe and usable. The help, including kitchen, laundry and care-takers showed no evidence of being the source of the infection. Later, as mentioned above, it was learned that the child admitted to the quarantine ward had had a typical attack of dysentery six weeks prior. The first two cases stricken had spent two weeks in quarantine with this case. These three children took sick on June 4, 5 and 6, respectively. A fourth case, a baby, took sick June 12 and had only come in contact with the nurse and two of the above cases, the other being isolated on account of measles. The remainder of the cases were taken sick about this time—none later than June 14. The severity of these varied from slight to marked attacks, one care-taker being very ill.

The three cases mentioned above as contracting the disease from the original were all that we had an opportunity to study and a short account of each is given.

Case 1.—Frank, aged 6 years, took sick on the night of June 5, with a fairly sudden onset. Vomited slightly, had bloody, mucus stools and passed into a comatose condition. There was some pain. The temperature ranged around 103 F. The bacillus to be described was obtained in almost pure culture on plain agar plates four or five days after the onset (first examination). The leukocyte count at this time was 17,500, and the patient's serum did not agglutinate the organism. June 20th the leukocyte count was 12,500, with negative serum reactions. June 24th, however, the serum gave positive agglutination reactions in dilutions of 1-20 and of 1-40 at the end of thirty minutes. Control serums were negative at the end of two hours with all the above tests. The temperature at this time was normal and the white count was 6,000. Patient recovered.

Case 2.—Philip, aged 4½ years, took sick June 6, and ran a course similar to that of Case 1. The temperature was lower, but the exhaustion was as great. The organism was

obtained from the stools about the fourth day (first examination) and again on the eighth day. The leukocyte count at this time was 18,500 and serum reactions were negative. June 20, the leukocyte count was 12,000 but now the agglutination reactions in dilutions of 1-20 and 1-40 were positive. On June 24 the leukocyte count was 7,200 again with positive agglutination in dilutions of 1-20 and 1-40 and also 1-80. Higher dilutions could not be made, because of lack of serum. Control serum reactions were negative in each instance. Patient recovered.

Case 3.—Baby Eveylin, aged 9 months, took sick June 12, just seven days after being exposed to the two previous cases. The attack was very severe. Leukocyte count on second day of disease was 4,000. Agglutination reaction was negative. Child was removed to the Children's Hospital where it died on the seventh day of the disease. The organism was recovered from the stools at two different examinations. A further study of the child was impossible.

The organism found in the stools on repeated examination of each of these three cases is a short rod, similar to the bacillus typhosus in size and form, Gram negative, non-motile, produces acid in milk, rarely coagulates milk or not until late. It forms indol slightly in Dunham's peptone solution. It produces acid and gas on the following sugars and in increasing amounts in the order mentioned: saccharose, dextrose, maltose, lactose and mannite. Being a mannite fermenter and an indol producer it is at once thrown out of the Shiga group of dysentery bacilli.[1] It probably falls in the Flexner group of dysentery bacilli rather than in the colon group, since the colon bacillus does not always ferment saccharose, usually produces indol in large amounts, curdles milk ordinarily within forty-eight hours and is usually motile. The organism gave positive agglutination reactions at fourteen days and nineteen days after the onset of infection in the two cases studied. A further study of this bacillus is being made on laboratory animals as regards serum reactions and pathogenicity.

October 14, 1912.

1. Hiss: Jour. Med. Res., 1904, 13, p. 12.

A SPECIFIC IMMUNE SERUM LIPASE AND ITS RELATION TO SPECIFC SERUM HEMOLYSIS

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By the observations of several experimenters (Kurt Meyer, Citron and Reicher, Bergel, and others) the antigenic properties of lipoids and other fatty substances have been established. Therefore, we are no longer forced to go to protein compounds or substances for antigenic material. Other investigators (Neuberg and Reicher, Neuberg and Rosenberg) have pointed out a close parallelism between hemolytic and lipolytic agents and have considered whether hemolysis is a kind of lipolysis, or, at least, whether the lipolytic activities of a hemolysin play a direct and essential part in its functioning.

Bergel has recently shown that the serums of animals immunized to foreign red cells are about twice as active in splitting such substances as lecithin, ethylbutyrate, butter fats, etc., as the serums of the same animal before treatment. These are alien fats and lipoids, the specificity of this increased lipase not being considered.

By experimental procedures we undertook to determine whether this newly formed lipase was specific for the antigenic substances used and, also, the part it plays in hemolysis. Hen corpuscles were incubated with a specific hemolytic serum in various combinations, with and without complement, boiled and titrated for acidity with a weak alkali. An acidity was found here which was not produced by various other serums with the hen corpuscles or other corpuscles with the anti-hen serum. The acids thus produced were readily extracted with ether.

It was concluded, therefore, that hemolytic serum contains a lipase specific for the cells used in its production.

To determine the relation of this immune serum lipase to sensitization of corpuscles, hemolytic serums of high titer were diluted with nine parts of 0.85 per cent. sodium chlorid and heated in a water bath for thirty minutes at 70 C. The heated serums were found to be specifically hemolytic but they had lost their lipolytic action, both specific and non-specific. Hence the lipase content of a hemolytic serum is not essential to its hemolytic action.

This, however, does not eliminate all lipolytic action in a hemolytic system, since a non-specific lipase is always present in the fresh guinea-pig serum used as complement. So various methods (heat, chemical, complement-splitting, etc.) were employed in an effort to separate the complement and lipase of fresh serum. We were not able to do this by any of the methods used and a lipase-free hemolytic system was, therefore, not established.

In the course of these experiments it was observed, however, that the lipase action and complement strength of several different serums were closely parallel and that the entire lipase of a serum remains in the "Endstück" fraction of so-called split complement.

CONCLUSIONS

1. Certain lipoids and lipoid combinations act as specific antigens.

2. The increased serum lipase which occurs on immunization of animals to foreign red cells is, at least in part, specific.

3. This specific lipase is not essential to hemolysis.

4. Serum lipase is found in the "Endstück" of split complement.

5. There is a parallelism between the complement strength and lipase content of the serums of different animals (man, rabbit, guinea-pig, sheep, ox, cat).

(A complete report of the experimental data will be found in the *Journal of Experimental Medicine*.)

October 14, 1912.

INTRAVITAM STAINING OF TUBERCULOUS GUINEA-PIGS WITH FAT-SOLUBLE DYES *

HARRY J. CORPER

Fat dyes administered under various conditions to guinea-pigs with tuberculosis never were found within the tubercles. This is in favor of the view that the fats of the tubercle are derived from the intracellular fats of the tissues forming the tubercle, and not from food fats or transported depot fats.

Tubercle bacilli within tubercles in such animals do not become stained with the fat stains.

Saturation of the animal with common fat dyes has no noticeable influence on the course of a tuberculous infection in the guinea-pig.

The fat stains employed in these experiments (sudan III, scarlet R, sudan yellow, sudan brown, Nile blue sulphate) were never found to stain any but depot fats, not being present in the parenchymatous cells, whether normal or diseased. They caused no apparent harm to the guinea-pigs even after being fed over 200 days.

Subcutaneous or intraperitoneal injection of fat dyes dissolved in fats and oils is much less effective in staining the depot fats than is feeding the stained fats.

Nile blue sulphate is toxic when given by injection, and when fed it did not cause staining of the fat tissues. Sudan yellow also failed to stain the fat tissues and is excreted by the kidneys. Sudan brown has little or no effect on the fats. Scarlet R gave a more intense coloration than sudan III but in general the effects are about the same.

Fat dyes do not pass through the guinea-pig placenta to the fetus, or at least the fat of embryo pigs from stained mothers is not stained (corroborating the Gages,

* The full report of this work will be found in the Journal of Infectious Diseases, November, 1912.

Mendel and Daniels). The embryos often show extremely fatty, but unstained livers. Fat dyes were never observed to pass into the milk of lactating guinea pigs, although positive results have been obtained by others.

October 14, 1912.

THE FORMATION OF HYDROCHLORIC ACID ON THE FREE SURFACE AND NOT IN THE GLANDS OF THE GASTRIC MUCOUS MEMBRANE

R. R. BENSLEY AND B. C. H. HARVEY

The human gastric juice contains 0.58 per cent. of hydrochloric acid.[1] The parietal cells have been suspected of forming it, but there has been no definite evidence showing that they actually do form it. The occurrence of Prussian blue sometimes in the canaliculi of a few parietal cells near the lesser curvature, after the injection of solutions of iron and ammonium citrate and potassium or sodium ferrocyanide, has been interpreted as proving that free hydrochloric acid was formed in the parietal cells in general.[2]

By injecting these solutions, we found the Prussian blue in many places other than these few parietal cells. Our results show that it is formed in the blood and lymph vessels of the stomach; that it appears in them and on the surface before it appears in any parietal cells; that it appears also in many parts of the body—liver, spleen, intestinal epithelium, etc. Its appearance cannot be due in all these places to the formation of free hydrochloric anid, therefore its presence in a few parietal cells does not prove that there is any free hydrochloric acid in them, whereas its absence from most of the parietal cells even when present in so many other places, sug-

1. Rosemann, R.: Beiträge zur Physiologie der Verandung, Arch. f. d. ges. Physiol. d. Mensch. u. d. Tiere, 1907, cxviii.
2. Fitzgerald, M. P.: The Origin of the Hydrochloric Acid in the Gastric Tubules, Proc. Roy. Soc., 1910, B, 83.

gests strongly that they do not form free hydrochloric acid. The presence of the reaction in parietal cells probably indicates reduced vitality or death of the cells. We found, after the injection of these salts, combined with injury to the mucous membrane by surgical operations on it, that dead parietal cells were always filled with Prussian blue, and that injured ones took up more of it than uninjured ones.

The results obtained with the Prussian blue reaction being thus unsatisfactory, we turned to other indicators, hoping to find some that would combine with the content of the gland lumina and parietal cell canaliculi while the gland was still alive.

Solutions of the bichlorid of cyanamin are blue in the presence of acid, even in 1/600 of the concentration present in the gastric juice. They are red with alkalies (free base), and intermediate in tint in neutral solutions (monochlorid). When bits of living, actively secreting mucous membrane are placed in saturated solution of cyanamin bichlorid in salt solution and allowed to remain a few minutes the secretion content of the parietal cell canaliculi is stained red (alkaline), that of the gland lumina is bluish-red (neutral), whereas at the bottom of the foveola there is a sudden change to intense blue (acid) which extends over the free surface. Similar results were obtained with phenylated Nile blue, with Nile blue sulphate and with several other compounds, all of which are indicators of alkalinity.

Neutral red solutions are red with acids and yellow with alkalies (precipitated base). When bits of living, active mucous membrane are placed in a solution of one part of neutral red in ten thousand parts of physiologic salt solution, the contents of the canaliculi are yellow (alkaline), those of the gland lumina are orange (neutral) and at the bottom of the foveola appears the intense red (acid). After some time the cells die in the solution and all become acid.

These four consistent results, and the number mentioned might be increased several times over, show that the hydrochloric acid first exists in the free state in the foveola. There is no acid in the gland. There is

an alkaline substance in the canaliculi of the parietal cells. Therefore only the antecedents of the acid are formed within the glands. These are probably organic chlorids, since Greenwood[3] and Macallum[4] have shown that chlorids are relatively abundant in the parietal cells.

These facts afford a simple explanation of why the healthy living stomach does not digest itself, for in the absence of acid there is probably no pepsin, but only pepsinogen, present. Pepsin is destroyed by alkalies while pepsinogen is not affected by them.

Further, the contents of parietal cell canaliculi and of gland lumina are relatively rich in solids. At the bottom of the foveola the secretion appears to be diluted, and then speedily to become acid.

November 11, 1912.

THE PARS INTERMEDIA: ITS RELATION TO DIABETES INSIPIDUS

DEAN LEWIS AND S. A. MATTHEWS

Polyuria is frequently noted with tumors surrounding the infundibulum and invading the interpeduncular space. It is associated with 7 per cent. of the cases of Fröhlich's syndrome. One of the most common tumors found in the interpeduncular space and associated with this syndrome develops from inclusions of mouth epithelium situated along the anterior surface of the infundibulum. These tumors must cause symptoms by pressure on the adjacent structures, for the cells composing them have no secretory activity. Some believe that they cause symptoms by pressure on certain hypothetical centers in the floor of the third ventricle, a view generally discredited since the physiology of the hypophysis has been more carefully studied.

3. Greenwood, M.: Observations of the Gastric Gland of the Pig, Jour. Physiol., 1885, v, 195.

4. Macallum, A. B.: Die Methoden und Ergebnisse der Mikrochemie in der Biologischen Forschung, Ergebnisse d. Physiol., 1908, vii, 628.

Kahler in 1886, in analyzing twenty-two cases of diabetes insipidus, found the lesion in seven of these about the infundibulum, the substantia perforata posterior or the corpora mamallaria. Most of the attempts at artificial production of diabetes insipidus have been confined to injuries of the floor of the fourth ventricle and the cerebellum. Attempts to produce diabetes insipidus in this way were stimulated by the work of Claude Bernard, who showed that puncture a little anterior to the glycosuric center caused a polyuria, the urine in most of the experiments performed by him containing albumin but no sugar. Eckhardt later verified these experiments, and also produced polyuria by injuring one of the lobes of the cerebellum to which he gave the name of "lobus hydruricus."

Polyuria produced by this puncture is not permanent. By injecting silver nitrate solution Kahler produced a polyuria which lasted for some weeks. Finkelnburg has recently repeated these experiments. He produced a definite polyuria in but six out of sixteen cases in repeating Kahler's experiments. In this form of polyuria, as Finkelnburg points out, the specific gravity of the urine is not greatly reduced and the kidney is still able to secrete a concentrated urine.

Meyer believes that in diabetes insipidus there is a disturbance of renal function, the kidneys being unable to secrete a concentrated urine. The observation made by Herrick on a patient suffering with diabetes insipidus would seem to be an argument against Meyer's theory, for in this case a highly concentrated urine was passed after a spinal puncture was made.

The demonstration by Magnus and Schäfer of a diuretic substance in the posterior lobe of the hypophysis which is independent of the pressor substance has stimulated investigations as to the possibility of hypersecretion of the pars intermedia being the etiologic factor in the production of diabetes insipidus. The frequent association of polyuria with lesions of the base of the brain and interpeduncular space would indicate the importance of the pars intermedia in the production of diabetes insipidus.

This report, which is preliminary, deals with eighteen experiments in the attempts at producing diabetes insipidus experimentally. Dogs were used as experimental animals. The hypophysis was approached by the buccal route after the method of Aschner. In nine of these eighteen experiments a marked diuresis was observed, the urine containing neither albumin nor sugar. In nine of the animals no polyuria was noted following the operation.

The two following experiments are cited to indicate the character of the polyuria induced by hypophyseal injury:

Experiment 6.—Dog weighing 6 k. was operated upon Sept. 24, 1912, and killed Oct. 1, 1912. The animal was in good condition one week after the operation and had apparently fully recovered from the operation.

Sept. 24-25	passed	1,000 c.c.	1,002
Sept. 25-26	passed	2,100 c.c.	1,001
Sept. 26-27	passed	1,900 c.c.	1,002
Sept. 27-28	passed	1,100 c.c.	1,003
Sept. 28-29	passed	700 c.c.	1,010

The wound following the injury was practically healed although there was some fibrin about the floor of the third ventricle.

Experiment 10.—Dog weighing 4½ k. operated Oct. 6, 1912, and killed Oct. 12, 1912. The day following the operation the general condition of the animal was good. Hypophysis exposed and injured with a cautery.

Oct. 6- 7	passed	2,450 c.c.	1,000
Oct. 7- 8	passed	3,900 c.c.	1,000
Oct. 8- 9	passed	900 c.c.	1,007
Oct. 9-10	passed	300 c.c.	1,012

In both of these cases the anterior lobe of the hypophysis had been destroyed. In one case, in which no polyuria was observed, the anterior lobe was gone, but the greater part of the pars intermedia appeared to be intact. This animal was chloroformed because he had commenced to show definite symptoms such as arching of the back, curling of the tail beneath the body and general soreness. The hypophysis had been destroyed

and there was no extensive injury of the floor of the third ventricle. ibrin was found posteriorly over the dura of the basilar process with no extension to the leptomeninges. There was a localized internal pachymeningitis.

In none of the nine in which polyuria has developed after injury of the hypophysis has the urine contained albumin or sugar.

Serial sections through the floor of the third ventricle from eighteen animals have been examined. The blocks of tissue were fixed in Zenker's fluid and stained with hematoxylin and eosin; no differential granule stains being used. As stated above, nine of the animals had no polyuria following the operation, while the other nine had a polyuria varying from 500 to 5,000 c.c. during the first twenty-four hours and which lasted from three to five days.

In the nine specimens removed from animals without polyuria the lesion varied. In two (5 and 16) the anterior lobe was injured. In one of these the changes were limited to the anterior inferior part of the anterior lobe and the pars intermedia was intact. In the other there was some hemorrhage into the cleft and the capillaries of that part of the pars intermedia attached to the floor of the third ventricle were dilated, but there were no definite cellular changes in the epithelium of the pars intermedia. In two of the specimens (12 and 35) the removal was complete, no traces of pars intermedia being found. In both of these the removal had been clean, there being but a small amount of fibrin and old blood clot at the site of operation. In the fifth specimen (17) the removal had been complete and the operation had been extended so as to involve the third ventricle, a wax plug being inserted into the cavity with the view of determining whether mechanical injury of the third ventricle would cause a polyuria. There are no traces of pars intermedia in this specimen. The nervous tissue adjacent to the site of injury shows considerable inflammatory reaction. In four of the specimens there are remnants of pars intermedia. In specimens 10 and 14 the remnants of pars intermedia are

very distinct. In Specimen 10 they are surrounded by considerable fresh blood, but there are no regressive changes in the cell. One might think from the histologic appearance that this animal would have had a polyuria. In Specimen 14 there is a relatively large amount of pars intermedia in the cells of which distinct karyokinetic figures are seen. Evidently the pars intermedia in this case is proliferating rapidly. On either side of the pars intermedia, and even invading it and superjacent nervous tissue, is an inflammatory exudate. This animal presented marked constitutional symptoms from the first. In Specimen 32 the remaining pars intermedia is badly broken up and surrounded by a blood clot, while in Specimen 24 the remnants of pars intermedia are displaned to one side with the broken stalk. There is no capillary dilatation in the remnant of tissue.

In the nine specimens removed from animals which had a polyuria there are distinct remains of the pars intermedia in all. In Specimen 18, removed four weeks after operation, there is a large mass of pars intermedia lying perfectly free and not surrounded by a blood clot or inflammatory exudate. In this case a wax plug had been inserted into the floor of the sella and had been made to protrude into the floor of the third ventricle with the idea of producing a continuous mechanical pressure. When this specimen was removed the floor of the third ventricle was covered by a layer of delicate, velvety tissue resembling pars intermedia. There has been apparently a complete removal of the anterior lobe, although scattered throughout the acini of the pars intermedia are a few cells which take the eosin stain, the cytoplasm, however, staining diffusely.

In Specimen 29, removed from an animal which presented the most marked polyuria, passing during the first twenty-four hours 5,000 c.c. of urine, there is a large amount of pars intermedia, the cells of which take a much heavier stain than ordinarily. To one side of the pars intermedia which is left is a small blood clot, which, however, is not intimately related to the remnant of pars intermedia which is left.

In the remaining seven specimens there are also remnants of pars intermedia. In these cases with polyuria the pars intermedia does not show the same degree of mechanical injury as do those in which polyuria was not noted; the cells in all these cases preserving nearly normal characteristics.

In some of these instances there has been some injury of the floor of the third ventricle but the evidences of injury have consisted of little more than a capillary dilatation. In Specimen 21 the anterior lobe was injured with a cautery. The greater part of the lobe was destroyed, a large hemorrhage occurring into it. The margins of the lobe were not destroyed although many degenerating eosinophil cells are found. The vessels of the pars intermedia are widely dilated and some hemorrhage has occurred. These changes are most marked at the transition zone between the anterior lobe and the pars intermedia, but capillary dilatation is also found at the floor of the third ventricle. Hyaline bodies are found in these cases in the nervous tissue of the floor of the third ventricle but they are not more abundant than in the normal dog.

In all of the nine specimens removed from animals which had a marked polyuria, there are distinct remnants of pars intermedia, which histologically appears to be in good condition. As stated above, remnants of pars intermedia were found in four animals which had no polyuria. In one of these there are distinct evidences of a marked inflammatory reaction about the pars intermedia and the animal presented general symptoms from the beginning which undoubtedly would have abolished or modified a polyuria. In two other cases in this group the remnants of pars intermedia were badly damaged, being surrounded by a fairly large blood clot. In one the remnant of pars intermedia was in good condition and one would have judged from a histologic examination that the animal from which this specimen was removed would have had a polyuria.

Total removal of the hypophysis is not associated with polyuria, neither is injury of the anterior lobe proper, the pars intermedia being intact. The most constant

finding in all the animals with a polyuria is a remnant of pars intermedia. Injury of the transition zone, accompanied by dilatation of the capillaries of the pars intermedia also causes a polyuria.

The polyuria has not lasted over five days and in some cases the amount of urine secreted has became rapidly reduced in amount after the second twenty-four hours.

While we have been unable to produce a permanent polyuria, we believe that the polyuria incited by hypophyseal trauma resembles that of diabetes insipidus more closely than that produced in any other way experimentally. The regularity with which the polyuria can be produced by stimulation of the posterior lobe of the hypophysis and infundibulum and the properties of the urine excreted would suggest the diabetes insipidus is dependent on hypersecretion of the diuretic substance of the posterior lobe, which is secreted by the epithelial covering known as the pars intermedia.

Clinical and experimental evidence would seem to indicate that diabetes insipidus is due to hypersecretion of the pars intermedia.

Nov. 11, 1912.

VITAL STAINING OF TUBERCLES

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This is a preliminary report of experiments undertaken with the hope that some dye might be found that could be used without injury to the animal and which would penetrate the tubercle and have a curative influence on it. A few reports have recently been published concerning the relation of certain dyes to the tubercle, but mostly with the view of discovering the origin of the tubercle and studying its histogenesis. In this work, the following questions have been constantly before me:

1. Will the dye penetrate the tubercle?

2. Is it non-toxic to the animal tissues? Can it be used for long periods without injury to the animal?

3. Will it penetrate and stain the individual tubercle bacillus?

4. If so, does it kill the bacillus or at least inhibit its growth?

5. If it has in itself no bactericidal power, can it enter into combination with other chemical substances which may increase its bactericidal power without making it more toxic for the animal or altering its penetrating power?

Some experiments have been made with the following dyes, although not all are yet ready to report: trypan blau, trypan roth, isamine blau, pyrrhol blau, methylene blau rectificiert n. Ehrlich, methylene blau medizinisch pur, pharmacopeial methylene blue, seven kinds of new methylene blue, brilliant kresyl blau, pyronin, neutral red, janus green, gentian violet, basic fuchsin, eosin A, eosin blau, erythrosin and bismarck brown.

Of all these dyes, trypan blau has been most thoroughly tested, having been injected into sixteen tuberculous guinea-pigs and also tested for its staining and bactericidal power. It readily penetrates the smaller tubercles, staining the central necrotic area and the peripheral zone of granular cells, leaving a middle fatty zone nearly dye free. It less readily penetrates to the caseous or purulent centers of large tuberculous glands, but will stain this mass deep blue if injections are repeated several times. It is difficult, however, and usually quite impossible to find stained tubercle bacilli in this mass, although carbolfuchsin stain will show that they are present in large numbers.

The dye can be used in large doses and at frequent intervals for a long time without noticeable injury to the animal.

On a slide or on agar slant it stains groups and masses of tubercle bacilli very well, but individual bacilli not at all or only faintly.

It does not kill tubercle bacilli, since cultures exposed to the dye even for forty-four hours and then injected

into guinea-pigs quickly caused a local and generalized tuberculosis. Nor does it inhibit their growth, since they grow readily and luxuriantly on agar which is deeply stained with the dye.

The fifth question regarding its possible use as a carrier of a more bactericidal substance into the tubercle can not be answered yet, but experiments are now in progress which will, I hope, furnish an answer to this question and which will be reported later.

Trypan roth also penetrates the tubercle readily, as was also shown by Lewis, and it is practically innocuous. On the slide or on agar culture, it stains the bacilli but faintly, however, and does not kill them nor inhibit their growth. In the animal body, no stained bacilli have been found.

Isamine blau and pyrrhol blau, so far as tested, are very similar to each other and resemble in their action trypan blau, but are slower and weaker.

The methylene blues all penetrate the tubercle and in small doses are well borne by the animal. They all readily penetrate the tubercle bacillus outside of the animal body, staining it deeply and permanently. They all seem to have some bactericidal influence on the tubercle bacillus, since I have not succeeded in getting growth on agar tubes stained with these dyes and some of the animals inoculated with the stained bacilli have not developed local tubercles. Other experiments intended to verify these results and still others to test the curative influence of these dyes in experimental tuberculosis in animals are in progress and will be reported later.

The eosins and erythrosin, basic fuchsin and gentian violet readily penetrate and stain the individual tubercle bacilli and have inhibited their growth on agar. They have not, however, killed the organism, as animals inoculated with the bacilli stained with these dyes, readily developed the disease.

As to the curative value of these dyes and also of the other dyes on my list, the results of experiments now in progress will be reported later.

November 11, 1912.

A RAPID METHOD FOR MAKING CELLOIDIN SECTIONS

MAURICE BUCHSBAUM

Herxheimer's[1] quick celloidin method takes twenty-four hours. The tissues are fixed in formalin or alcohol, then placed in pure acetone in the incubator at 37 C. for ½ to 1 hour. This is followed by thin celloidin for 4 to 5 hours, and thick celloidin for 2 to 3 hours. By Cullen's[2] method permanent specimens from frozen sections may be obtained by previous formalin fixation in from 15 minutes to 3 hours. This would be the method of choice if it could be employed advantageously in the examination of very soft and finely divided material as uterine scrapings, epithelioma, from the meshes of which microscopic particles and cellnests are apt to drop out "as there is nothing to hold them *in situ* as when celloidin is used." Frozen sections do not stain so readily, and very often become distorted in the handling. However, the freezing microtome has its field of usefulness where quick diagnosis is paramount over nicety of appearance. I do not offer my method as a substitute for this, but rather as an aid to the pathologist and surgeon to facilitate a histologico-pathologic diagnosis when pressed for time.

The principle of my method consists in shaking the specimen in contact with the fluid reagents. The agitation thus brought about within the fluid dislodges the air-bubbles confined within the meshes of the tissue and prevents the formation of a coagulation membrane and thus allows the reagent to act simultaneously, both centrally and peripherally. With the usual method the fixing and hardening is delayed because of the formation of a coating of albumin on the surface of the specimen; this coat of albumin then acts like an osmotic membrane and the reagents penetrate slowly through it by osmosis. The following are the steps:

1. Herxheimer: Technik der Pathologish-histologischen Untersuchung. 1912.
2. Cullen: Bull. Johns Hopkins Hosp., April, 1895, and May, 1897.

1. Small pieces of tissue from 0.5 to 1.5 c.c. are placed into 50 c.c. of a freshly prepared formalin solution (formalin 1 part, physiologic salt solution 3 parts) and vigorously shaken from 1 to 3 minutes.

2. Remove specimen into 30 per cent. alcohol and shake for 30 seconds. (In this the formalin is removed and the hardening process begins.)

3. Transfer into 80 per cent. alcohol for 1 minute and shake for 30 seconds.

4. Into a absolute alcohol for 5 minutes and shake for 1 minute.

5. Alcohol and ether for 4 minutes.

6. Celloidin No. 1 for 5 minutes, shake 1 minute.

7. Celloidin No. 2 for 5 minutes, preferably in incubator at 37 C., shake for 1 minute.

8. Celloidin No. 3 for 10 minutes, shake for 1 minute then place bottle in incubator.

9. Blocking. Expose to the air for 1 minute on the block, then place in chloroform from 3 to 5 minutes.

10. Alcohol 80 per cent. until ready to cut. Stain as usual. The sections thus prepared stain beautifully with hematoxylin and eosin and keep permanently.

The whole process takes from 45 minutes to 1 hour.

November 11, 1912.

ATRESIA OF THE ESOPHAGUS WITH TRANSPOSITION OF THE VISCERA

WILLIAM PETERSEN

Atresia of the esophagus is not an uncommon anomaly, some seventy-five or eighty cases having been reported to date. The occurrence together with a transposition of the viscera is, however, rather unusual; I have been able to find but three similar cases in the literature. The esophageal anomaly in most of the cases reported is similar in anatomic structure, consisting of a rather short pouch-like cephalic portion of the esophagus, ending blindly at about the bifurcation of the trachea. A

more or less rudimentary lower portion then connects with the trachea either at the bifurcation or lower down with one of the bronchi.

This child was born in the maternity service of Dr. Simon at the Michael Reese Hospital. The delivery was normal. The child was suffering from asphyxia, quickly relieved by the removal of mucus from the throat. Attention after birth was directed to the child because of persistent regurgitation of its nourishment, and the frequent attacks of asphyxia due to the accumulation of mucus in its throat. On examination it was found impossible to pass a bougie down the esophagus, and the stomach was observed to fill with air with each swallowing movement. A diagnosis of atresia of the esophagus was made. The child was put on rectal feeding. It died six days after birth.

At autopsy the anomalies already referred to were found. The transposition of the viscera was not complete, those organs developing in the dorsal mesentery, i. e., pancreas and spleen, being found on the left side. The pylorus was directed to the right side, although the stomach was also on the right side. The left testicle was undescended.

Numerous explanations have been offered to account for the esophageal anomaly. The older ideas of prenatal inflammatory changes, and faulty arterial development are untenable because of the marked uniformity in the anatomic structure of the atresia. Dr. Zeit has recently advanced the most plausible explanation, believing that the anlage for the tracheo-esophageal septum instead of occurring from the anterior wall of the upper part of the archenteron, occurs from the posterior wall. Giffhorn's view is that there is faulty closure of the lower part of the tracheo-esophageal septum, leaving the connection between trachea and lower part of the esophagus, while adhesions close the upper part of the esophagus. In view of the fact that the esophagus during the developmental stage has a very irregular lumen, such adhesions might easily occur. There is also a possibility that the chief center of growth of the tracheo-esophageal septum might begin in the center of the wall

of the archenteron and extend both upward and downward in an equal direction. In this way the upper portion of the gut would become closed posteriorly, leaving an incomplete portion below. In this case one must assume that there is some downward growth of the upper esophageal pouch.

November 11, 1912.

PRELIMINARY NOTE ON THE RÔLE OF MAGNESIUM IN SUGAR FORMATION

ALFRED C. CROFTAN

A study of plant metabolism is destined to throw light on animal metabolism, the latter representing an evolution of the former, an adaptation to changed conditions of life rather than a fundamentally different process. The boundary between the two is in some regions indistinguishable. Perversions of animal metabolism in some of their phases no doubt represent a reversion to a more primitive, i. e., a vegetable type; hence an understanding of plant metabolism should aid in the interpretation of disordered animal metabolism.

The conversion of CO_2 to carbohydrate is characteristic of plant life and constitutes the most important step toward converting inorganic into organic material and rendering it available for animal food. Chlorophyll under the influence of sunlight, we are taught, produces this conversion, while a volume of oxygen is at the same time exhaled that approximates the volume of carbon dioxid absorbed. At the photosynthetic centers formaldehyd has been found and it is probable that by polymerization this is converted into sugar and starches. Green leaves in which all protoplasm and enzymes have been killed by boiling in water are still capable of converting CO_2 to formaldehyd in the presence of light,[1] hence this process is not "vital."

My studies are based on the discovery of Willstätter and his pupils[2] that chlorophyll contains a large propor-

1. Usher and Priestley: Proc. Roy. Soc., 1906, series B. 77, 369.
2. First paper, Ann. 350, p. 48.

tion of magnesium. In looking through the literature regarding the action of CO_2 on Mg it was found that Mg reacts differently from other chemically related metals. Thus a slow stream of CO_2 passing through water holding amalgams of sodium, potassium, barium, aluminium in suspension leads to the formation of formic acid (formates) but magnesium treated in a similar way does not lead to the production of formic acid or formates. Whereas in the case of all the other metals studied no formaldehyd was formed, a considerable quantity of the aldehyd is generated with Mg. This process, I was able to show, occurs as well in the dark as in sunlight. Fenton,[3] the discoverer of this fundamental fact, in a personal communication describes the following simplest technic: "Into a large bottle holding, say 3 or 4 liters (e. g., a "carboy") introduce about an ounce of Mg powder. Just cover the powder with water and then fill the vessel with CO_2. Close the vessel and leave it for twenty-four hours or more; filter and test liquid by Rimini's test (or by gallic acid, etc.)." I am inclined to believe that formic acid is formed as the intermediary step, the latter being promptly reduced to formaldehyd by magnesium.

Here, too, magnesium occupies a unique position for it appears to be the only metal of the many I have investigated so far that promptly reduces formic acid to formaldehyd. Fenton[3] found that a rod of magnesium dipped into a 10 per cent. solution produces considerable formaldehyd, dipped into ammonium formate solution hexamethylentetramine. Other metals investigated by me do not produce this reduction under identical conditions. For identifying formaldehyd I have used (aside from the colorimetric methods of Rimini, the gallic acid and the resorcin tests, recommended by Fenton) the reagent p-dihydrazinodiphenyl.[4] This substance can be kept in watery solution for months and reacts with formaldehyd alone in very dilute solution (reliable up to 1:6,000). Differentiation especially

3. Fenton: Tr. Brit. Chem. Soc., 1907, lxli, 687.
4. Emil Fischer: Ber. 9, p. 89, and Arheidt. Ann. 239, p. 208.

from other aldehydes and ketones is easy. The test is simple for the qualitative detection of minute quantities of formaldehyde and reliable for its quantitative determination.

It is interesting to note that among the gases generated by the violent reaction between magnesium and formic acid or formates is found oxygen. In view of the O-exhalation of plants this is suggestive. Qualitatively the emanation of O was determined by passing the gases evolved through a solution of alizarin-white, formed by the reduction, with NaOH and Sn, of alizarin-blue. This leuco body turns blue in contact with O; the possible action of atmospheric O was excluded by an "anaerobic" technic I adopted. This reaction has not yet been studied quantitatively.

Magnesium also plays an exceptional rôle in the conversion of formaldehyd to carbohydrates. Carbohydrate polymers of formaldehyd can be manufactured by most metal hydroxids acting on dilute formaldehyd solutions under proper conditions, but not by magnesium or its hydrate. Loew[5] has shown that at room temperature a 3 to 4 per cent. formaldehyd solution treated with a small quantity of freshly slaked lime is converted into sugar (methose, formose) within forty-eight to seventy-two hours. Magnesium hydrate does not produce this result even after months of standing. If calcium hydrate and magnesium are employed together, however, more sugar is formed. This is explained as follows: a solution of formaldehyd treated with slaked lime, according to Loew, leads to the formation of much sugar, some calcium formate and a little methyl alcohol. The proportion of formic aldehyd and of lime and the temperature conditions (see below) determine the relative amount of sugar and of formate generated. In the presence of magnesium much of the formic acid generated is converted into formaldehyd (see below) and thus more of the latter becomes available for polymerization to sugar. The reaction of Loew can be accelerated by gentle heat. A solution of formaldehyd, mixed with freshly slaked lime, is allowed to stand for one hour. No sugar practically is formed in this short time. The

5. Loew: Jour. f. pr. Chem., 33, p. 321.

solution is filtered and gradually heated to 63 C.; the solution clears rapidly and a sudden conversion of formaldehyd to sugar, almost quantitative, occurs. If the solution is heated rapidly and beyond 63 C. the conversion occurs violently with much ebullition and browning of the liquid takes place. Relatively very little calcium formate is formed by this method.

The sugar formed in this way differs from dextrose in cupric reducing power, degree of fermentability, polarization index and in its osazon; it is less sweet than dextrose, but is, in comparison to an aliquot amount of dextrose, remarkably well tolerated by diabetics of a certain type.

The presence of Mg in chlorophyll, with the possibilities in regard to its activities in formaldehyd formation and hence carbohydrate generation that the above data suggests, led me to investigate certain bile and blood pigments, that possess the same empiric formula as chlorophyll, for the presence of magnesia. The ordinary methods of manufacturing, e. g., bilirubin or biliverdin from bile or gall-stones all imply the use of acid, hence the separation of any Mg that might be present. By adopting a process of fractional precipitation in neutral or alkaline saline solutions similar to that employed by Willstätter in the manufacture of his chlorophyll (here too he warns expressly against the use of even weak acids) a product is obtained that contains a considerable proportion of magnesium.

One can imagine, therefore, that iron-free magnesium pigments play a rôle in the animal economy corresponding to the rôle played by similar magnesium pigments in the more primitive phases of plant economy. One can imagine that the preeminently reducing properties of magnesium manifested, e. g., by the conversion of carbon dioxid (CO_2) to formaldehyd (CH_2O) become operative in the animal economy (the reducing qualities of animal tissues being well recognized) as well as in the plant economy, while at the periphery of the cells the iron-holding compounds operate in the direction of promoting oxydative phenomena.

January 13, 1913.

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TUBERCULOSIS OF THE STOMACH, WITH EXTENSIVE TUBERCULOUS LYMPHANGITIS *

KAETHE W. DEWEY

(From the Pathological Laboratory Rush Medical College, Chicago.)

This report of tuberculosis of the stomach was added to the long list of publications on the subject because the lesions were of a type very little discussed in the literature, because of the extensive involvement of the lining of the stomach and finally because the study of them resulted in a conclusion that they probably originated by retrograde infection of the lymphchannels. Theoretically this mode of infection has been generally admitted as a possibility but the evidence so far recorded is quite meager.

The lesions were numerous round and oblong nodules, forming ridges 1, 2, 3 and more cm. long, located chiefly along the lesser curvature on the posterior wall. Gross erosions or other defects of the mucosa could not be detected, although histologically some minute ulcerations were found in the nodular regions. The tuberculous nature of the process was confirmed by the finding of numerous tubercle bacilli. Besides the usual histological evidences of tuberculosis an increased number of lymphnodes and a state of hyperplasia in some of them was observed. Rows of lymphocytes were numerous just without thin-walled lymphchannels; in a few places collections of lymphocytes within them resembled beginning intimal tubercle formation. The anatomical distribution and grouping of the nodules and ridges strongly suggested the involvement of the lymphvessels, for in

* The complete paper appears in the Journal of Infectious Diseases, 1913, xii, 236.

both, location and arrangement, they corresponded to the perivascular lymphchannels of the coronary and the splenic group.[1]

In the literature on tuberculosis of the stomach there are no other reports of a tuberculous involvement of the lymphvessels without tuberculous ulcers. Przervoski[2] in his description of five cases of tuberculous ulcers of the stomach, mentions in three of them whitish ridges on the floor of the ulcers and extending from their borders. Histologically he describes a definite "lymphangitis tuberculosa" in these cases. The lymphogenic origin of tuberculous ulcers was assumed and discussed by Rosset,[3] who believes that the lesions described by Chiari[4] may possibly be interpreted as having such an origin.

November 11, 1912.

CONGENITAL ATRESIA OF THE SMALL INTESTINE

ALBERT HOWARD BAUGHER

(From the Laboratory of St. Luke's Hospital, Chicago, Ill.)

This specimen was taken at autopsy from a full term baby dying on the fourth day after birth with the clinical symptoms of intestinal obstruction. The baby weighed seven pounds and appeared normal when born. It nursed at the usual time, but soon became sick. It began to vomit at the end of eight hours and a little later the upper abdomen began to show some enlargement. It continued to nurse during the first twenty-four hours of life, but later was comatose. The vomit-

1. See descriptions of the lymph channels of the stomach by Sappey, Anatomie, Physiologie, Pathologie des vaisseaux lymphatiques, 1874; Most: Ueber die Lymphgefässe und die regionären Lymphdrüsen des Magens, Arch. f. klin. Chir., 1899, (59), 175; Cunéo et Delamare, Les lymphatiques de l'estomac, Jour. de l'Anat. et de la Physiol., 1900, (36, No. 4), 393; Poirier et Cunéo, Les vaisseaux lymphatiques, 1901; Polya und Navratil, Untersuchungen über die Lymphbahnen des Wurmfortsatzes und des Magens, Deutsch. Ztschr. f. Chir., 1903, (69), 421; Jamieson and Dobson, Lectures on the lymphatic system of the stomach, Lancet, 1907, (1), 1061.

2. Gastritis tuberculosa, Virchow's Arch., 1902, (167), 424.

3. Ueber einen Fall von tuberkulösem Magengeschwür. Mit besonderer Berücksichtigung der Genese. T. D. Freiburg i.Br., 1903.

4. Ueber einen Fall von Perforation des Magens durch tuberkulöse Lymphdrüsen. Wien. med. Wchnschr., 1878, (24), 650.

ing and tympanites gradually grew worse until death. At autopsy the abdomen was greatly distended and tympanitic, which was found to be due to a greatly distended duodenum and upper intestine, and also to a slightly distended stomach. Search was made for the obstruction, which was found at a point where the intestine ended in a blind pouch 60 cm. from the pylorus. The greatest diameter of this dilated portion of the intestine was near its distal end and measured about 6.25 cm. Passing upwards this diameter was practically maintained until about the beginning of the duodenum, where the diameter gradually lessened until the pylorus was reached and at which point it was 1.25 cm. The walls of this portion of the intestine were thicker than normal and were apparently uniform. Grossly this pouch might easily have been mistaken for a dilated cecum and colon. The visceral peritoneum at the point of obstruction was continuous with that of the blind pouch and the remainder of the bowel and formed a connecting cord 0.6 cm. long. This was the only point of visible constriction. Above this point there was a solid cone of tissue the base of which was 0.6 cm. in diameter, the altitude the same, and the apex of which was at the point of obstruction, and below the canal was patent for 5.0 cm. where a transverse membrane or septum completely occluded the canal; another occlusion was 2 cm. further down and still another 0.8 cm. from this point. These last two constrictions have a very small amount of solid tissue which helped to form the obstruction, but at the occlusion where the membrane was situated there was not even a trace of solid tissue. Below this point the canal was patent throughout. The mesentery presented no abnormality and there was no evidence of either acute of chronic peritonitis. The ileo-cecal valve was normal. Meconium and debris was distributed throughout the whole canal. All the constrictions occurred in a space of 8.5 cm. After the gas had been expelled from the stomach it was normal in size. The total length of the small intestine was 265 cm. and of the large intestine 38 cm. The jejunum by computation was 106 cm. (2/5 of small intestine), which would throw the occlusions into this division of the intestine.

I wish to thank Dr. Monahan and Dr. McClinton for the courtesy of allowing me to present this specimen. The patient was first seen by them in consultation on the third day.

January 13, 1913.

EXPERIMENTAL STREPTOCOCCAL ARTHRITIS IN RABBITS*

LEILA JACKSON

(From the Laboratory of St. Luke's Hospital, Chicago.)

The changes found in the microscopic preparations of the joints from seventeen rabbits injected intravenously with various strains of streptococci and living after inoculation for periods varying from two hours to four months, are briefly as follows: A few hours after inoculation bacteria appear in the capillaries of the synovial membrane, tendon sheaths and bone marrow in the neighborhood of the epiphyseal cartilages, in the latter sometimes occluding vessels. A little later the streptococci appear in the joint cavities surrounded by a small amount of albuminous fluid without cells and this is followed shortly by a more or less abundant cellular exudate. Multiplication of the organisms is rapid and is attended by more or less necrosis of the exudate, the tissues surrounding the joint cavities and tendon sheaths, the bone and bone marrow and epiphyseal cartilages. In the most severely affected joints there is almost complete necrosis of the exudate, synovial membrane, plicae synovialis and tissues immediately adjoining laterally and of the articular cartilages for from one-half to two-thirds their thickness. Accompanying these changes within and immediately about the joint cavity there is in many cases an infarct in the diaphysis of one or more of the long bones entering into the formation of the joint. These infarcts are triangular in shape usually with one side along the outer surface of the bone and the base close to the epiphyseal cartilage. These infarcts vary in size from 1.5-3 mm. long and 1-1.5 mm. across,

* The full article appears in the Jour. of Infect. Dis., 1913, xii, 364.

the latter representing from one-fourth to one-half the diameter of the bone at that point. Necrosis of the portion of the epiphysis bordering the epiphyseal cartilage is less frequent and once or twice dissection of the epiphyseal cartilage by a cellular exudate was observed. For the first three days there is almost no inflammatory reaction about necrotic tissues, but about the fourth or fifth day there is a definite cellular infiltration in the adjacent tissues laterally, the tendon sheaths and the lesions in the marrow. In the early stages of the reaction, especially where there is much necrosis, rather large numbers of polymorphonuclear leukocytes are present among the infiltrating cells, but where injury is slight and as healing progresses mononuclear cells predominate. These cells though having a rather uniform distribution in the tissues surrounding the joint cavities laterally are especially numerous about and within the walls of small blood vessels. Proliferation of the endothelium into the lumen of the vessels is also a common change.

Fairly typical small "rheumatic nodules" and vascular changes were found in the plica synovialis of a rabbit killed five days after inoculation, but multinucleated giant cells were not observed. A few multinucleated giant cells were found as early as eleven days after inoculation, but it is particularly in the later part of the healing process that the multinucleated giant cells and the typical nodules, such as I have described in the muscle of the rabbit's heart[1] and which are regarded as specific for rheumatism when present in the human myocardium, are found. Large numbers of plasma cells are also present in the infiltrated regions about the older affected joint cavities. The entire process, together with the nodules, giant cells and vascular changes, are of the same general character as those observed in the heart muscles of these same rabbits. It is believed that such differences as do occur are well accounted for by the differences in the type and structure of the tissues involved and especially the existence in the joints of a free surface which is nevertheless part of a closed cavity, whereas in the myocardium the bacteria are surrounded

1. Jour. Inf. Dis., 1912, xi, 243.

on all sides by compact tissues. In sections of the healed joints the synovial membrane and plicae synovialis appear quite normal, only an occasional small nodule being found in the plicae synovialis; but the healing of the articular cartilages apparently takes place less readily. Such reparative processes as I have observed are characterized by an irregular proliferation of cartilage cells or where the cartilage is entirely absent by the ingrowth of a vascular connective tissue. The processes of healing in the bone are apparently much more adequately carried out and the changes are similar to those observed in the healing of fractures.

February 10, 1913.

THE RELATION OF SPECIFICITY TO THE CHEMICAL COMPOSITION OF PROTEINS

H. GIDEON WELLS AND T. B. OSBORNE

A study of two similar, but chemically distinct, alcohol-soluble proteins (gliadin from wheat and hordein from barley) gives results which seem to be of significance in relation to the problem of specificity. Animals sensitized to one of these two proteins will react strongly if injected with the other, but not usually as strongly as if injected with the homologous protein. This indicates a common antigen in these two chemically similar proteins. But animals which have recovered from a reaction with the heterologous protein are still sensitive to the homologous protein, although now refractory to the heterologous protein with which they have just reacted, whereas animals reacting to the homologous protein become refractory to the homologous protein. These results establish the presence in each of these two proteins of at least two antigenic radicals; one which is common to both, and one which is specific for each. If these proteins are pure proteins, as all the chemical evidence shows, then these experiments establish that a single protein molecule may contain more than one antigenic radical demonstrable by the anaphylaxis reaction.

February 10, 1913.

EXPERIMENTS ON ANTIANAPHYLAXIS

KARL K. KOESSLER

(From the Memorial Institute for Infectious Diseases, Chicago.)

If animals, which have been sensitized to a foreign proteid, receive a sublethal dose of this proteid during the critical period, so that they recover from the toxic effects of the second injection, they are then rendered insusceptible to a third injection of even many times the multiple dose of the toxic proteid. This refractory state characterized by this inability to react has received by Besredka the name antianaphylaxis. Several explanations have been ventured of the underlying mechanism of this remarkable phenomenon. Of these the best founded seems to be the one of Friedberger, who ventures the opinion that the refractory state results from the impoverishment of the serum in antibodies which are used up for the neutralization of the protein introduced at the second injection. From this point of view and also for other reasons, it seemed of interest to study the curve of specific antibodies during the state of antianaphylaxis and to investigate if changes in the antibody content of the serum brought about at will by experiment would influence the state of antianaphylaxis.

A number of guinea-pigs were actively sensitized by the injection of 0.5 c.c. of a suspension of killed typhoid bacilli. Two weeks afterward the sublethal dose of a similar emulsion was determined and the animals were rendered antianaphylactic by the intracardial injection of this dose. Two of these guinea-pigs received ten times the lethal dose 48 hours later to prove that the animals were in fact in the state of antianaphylaxis. Daily determinations of the agglutinins and opsonins were made in the inactivated serum, beginning three days before the first injection. We used the method of antibody exhaustion in reading the endpoint of our experiments, following the suggestion of Dr. Hektoen, which furnishes a better comparative value for the study of antibodies than the usual determination of the opsonic index.

If we now observe the antibody content of one of our animals we see that the antibodies increase gradually after the first sensitizing injection, the effect of this injection being identical with that of a single immunizing dose. The use in the agglutinins and opsonins go nearly parallel and after small oscillations, reach a maximum, the maximum of the normal typical antibody curve usually attained between the eighth and eleventh day, following the first injection.

TABLE 1.—THE AGGLUTININ AND OPSONIN BEFORE AND AFTER ANAPHYLACTIC SHOCK IN GUINEA-PIG SENSITIZED WITH TYPHOID BACILLI

Days	Titer of Agglutinin	Extinction Opsonin	Notes
Days before injection—			
2	0	80	
1	0	80	
Day of injection—			
..	0	80	.5 c.c. typhoid culture.
1	0	100	
2	0	100	
3	0	200	
4	..	....	
5	0	200	
6	10	200	
7	80	300	
8	80	300	
9	50	300	
10	50	200	
11	50	200	
Days after first injection—			
12	50	200	Reinjection—shock.
12	0	50	30 m. after reinjection.
13	0	50	
14	0	10	
15	0	10	
16	0	10	
17	..	..	
18	..	10	
19	..	..	
20	..	..	
21	..	..	
22	..	..	
23	50	50	
24	50	50	
25	..	..	
26	50	50	
27	80	50	
28	..	..	
29	80	50	
30	100	50	
31	100	50	
32	....	..	
33	100	50	
34	100	80	
35	200	80	
36	200	100	
37	200	100	

At this period the animals received a second sublethal dose of killed typhoid bacilli, which rendered them antianaphylactic. This injection is followed by a sudden diminution of the antibody content in the serum, which, indeed, proceed to such an extent that the minimum reached seems to be inferior to the normal antibody content of the serum preceding the first injection. This sudden drop is first detected with our methods as early as one-half hour after the injection. As the table shows, the antibodies remain now at this low ebb for several weeks; thereafter they gradually increase until finally a height is reached approaching the acme of the first injection.

The duration of the low stage of the antibody content which characterizes the period of antianaphylaxis depends, as experiments show, on quantitative relations between the maximal quantity of antibodies obtained and variations in the amount of the second dose of antigen used.

At this stage animals again sensitized succumb to a renewed injection. The fact that the guinea-pigs are insensitive to a third injection as long as their antibody content is low suggested the idea of investigating whether the restocking of the antibody content would resensitize the animals and thus perhaps shorten the refractory period of antianaphylaxis. This can indeed be accomplished by the injection of an homologous immune serum, as first shown by Weil and Coca.[1] I used the serum of a rabbit immunized by repeated injections of killed typhoid bacilli which had an agglutinating titre of 1:2000. Two c.c. of the inactivated serum were injected intracardially in some of the antianaphylactic guinea-pigs. Two of the animals reinjected after 20 hours intracardially died with the typical symptoms of anaphylaxis, proving that the resensitization was complete. The antibodies following the injection of the immune serum increased very rapidly; within two to three days the antibody concentration reached a stage

1. R. Weil and A. F. Coca: An experimental study of antianaphylaxis. Proceedings of the Society for Experim. Biol. and Medicine, 1912, ix.

equal to the maximum reached following the first injection and in the subsequent days rose still above it.

TABLE 2.—THE AGGLUTININ AND OPSONIN IN SENSITIZED AND RESENSITIZED GUINEA PIG SUBJECTED TO TWO ANAPHYLACTIC SHOCKS

Days	Titer of Extinction Agglutinin	Opsonin	Notes
Before injection—			
2	0	80	
1	0	80	
Day of injection—			
..	0	80	Inj. with 0.5 c.c. typhoid cult.
Days after first injection—			
1	10	100	
2	10	100	
3	10	200	
4	..	..	
5	10	200	
6	10	200	
7	10	200	
8	50	300	
9	50	300	
10	50	200	
11	..	...	
12	50	200	
13	50	200	Reinj. 0.05 typh. culture; shock
13	0	50	
14	0	50	
15	50	10	
16	50	10	Inj. 2 c.c. antityph. ser. (rabbit)
17	80	80	
18	..	..	
19	100	100	
20	...	...	
21	...	...	
22	...	...	
23	200	300	
24	200	400	
25	...	...	
26	300	500	
27	400	200	Inj. 0.012 c.c. typh. cult.; shock
28	...	...	
29	0	...	
30	0	50	
31	0	10	
32	...	...	
33	50	10	
34	50	10	
35	50	50	
36	50	50	
37	50	50	
38	50	50	
39	..	..	
40	100	50	
41	100	50	
42	100	50	

;

The animals were again injected at this point with a sublethal dose and this injection was followed by a typical anaphylactic shock.

In investigating if the factor of time during the stage of antianaphylaxis plays any role in this resensitization, we found that the resensitization may be brought about at any number of days after the injection of the immune serum from 20 hours to several weeks. In this connection we observed two guinea-pigs of this series which were injected with immune serum in the third week after the second injection and died with symptoms of retarded anaphylaxis (only slight emphysema, but multiple hemorrhages all over the peritoneum and the intestinal mucosae). This rather startling observation that the injection of immune serum should prove fatal to two animals out of 16 resensitized seemed to warrant an explanation. The antibody content of these two animals was just beginning to increase (ops. 1/80, aggl. 1/50) when the injection of the immune serum occurred. Since every immune serum represents an antigen-antibody mixture it is possible that at the period of injection the animals had just enough antibodies to split free toxic protein contained in antigen of the immune serum, which resulted in the death of the animals.

That this phenomenon of the resensitization is absolutely specific and is only obtained with immune serum containing antibodies for the same antigen that was used in sensitization was verified by injecting antianaphylactic guinea-pigs of the same series first with normal rabbit serum and then with immune rabbit serum agglutinating micrococcus melitensis in a dilution of 1:1200. In neither case were we able to accomplish resensitization.

These results, then, indicate the following conclusions:

1. The antibody content of the serum during the whole period of antianaphylaxis is at its minimum.

2. The duration of the refractory stage is determined by the duration of this antibody exhaustion.

3. Antianaphylactic animals can be resensitized by the introduction of immune serum and we can shorten in this way the period of antianaphylaxis at will; and this resensitization is associated with an instantaneous rise in the antibody content of the serum of the resensitized animal.

February 10, 1913.

THE INHIBITIVE ACTION OF BILE UPON B. COLI

EDWIN O. JORDAN

These observations relate especially to the availability of bile media for the sanitary examination of water. My experiments have shown that pure cultures of B. coli, whether freshly isolated or long under cultivation, are inhibited in very considerable degree by fresh, neutral ox-bile. This inhibition may be observed in bile agar as well as in the lactose bile medium used in water analysis. Suspensions of B. coli in water for as long as one year show no greater proportion of cells inhibited than do freshly isolated strains. No evidence has been found that either fermentative or proteolytic qualities are weaker in those cells refusing to grow on bile media.

To summarize, these observations show: that bile inhibits at least from one-third to one-half of the viable cells of B. coli and sometimes a much larger proportion, that freshly isolated cultures are inhibited in at least the same degree as those under long cultivation or those subjected to prolonged sojourn in water, that there is no evidence that B. coli cells that are unable to grow on bile medium are any more "attenuated" or less "vigorous," biologically, than their fellows; and that with some care in making dilutions and in replating, if necessary, B. coli will be isolated in a larger proportion of cases from lactose broth fermentation tubes than from lactose bile. These facts may not modify the advantages claimed for bile media for presumptive tests, but they do demonstrate that bile is an inhibiting substance for B. coli as for other micro-organisms and that its use always involves the suppression of a certain number of viable cells. The cells that are suppressed cannot be assumed to be any less significant in the interpretation of sanitary water analyses than the cells actually surviving the passage through the bile.

February 10, 1913.

DIARRHEAL OUTBREAK POSSIBLY DUE TO PARATYPHOID INFECTION

KENNETH N. ATKINS

(From the Bacteriological Laboratory, University of Chicago.)

An explosive epidemic of diarrhea occurred in an orphan asylum in this city early in June, 1912. The clinical aspect of this epidemic has been reported by Drs. Baugher and Gay.[1] The epidemic was limited largely to the older children and adults in the institution. Forty-five per cent. of the older children, ages 6 to 10 years, two per cent. of the younger children, ages 1 to 6 years, and nine per cent. of the adults were infected.

Conditions at the institution—such as quarantine of new members previous to admission, separate but connected buildings for housing and separate toilet articles, etc.—make it impossible that this epidemic was caused by a "carrier."

All inmates of the home have the same food. City water is used in the institution. If milk had been the cause of this epidemic the percentage of young children sickened, who drink proportionately more milk than older children and adults, should have been larger than the percentage of older children and adults sickened.

On the day previous to onset of the epidemic, for the first time in the season, lettuce was served to all in the institution. Most of the older children and adults and few of the younger children ate lettuce. The use of infected lettuce would largely explain the distribution of this epidemic. The sickness of a laundress, who handled soiled clothes, and a baby fed on certified milk, but attended by the same nurse who was caring for two patients in the hospital, might have been caused by contact infection.

Paratyphoid organisms were isolated from feces of three children in the institution, from feces of the farmer on whose farm the lettuce used in the institution had been grown, from the contents of the farm privy and from soil of a lettuce bed on the farm. The farmer had been sick with diarrhea shortly previous

1. Baugher and Gay: Trans. Chicago Path. Soc., 1913, ix, 8.

to the outbreak of the epidemic in the institution. All of the paratyphoid strains isolated and studied agreed closely with one another in cultural characteristics and agglutination properties.

February 10, 1913.

A SAFETY RAZOR BLADE AS A MICROTOME KNIFE

VIRGIL H. MOON

Many new uses are being found for the safety razor blade. If some device is used for holding the blade and at the same time stiffening it, the safety razor blade becomes an excellent microtome knife, especially for use with the freezing microtome. A simple method for accomplishing this is as follows: The bit of an ordinary carpenter's plane is drilled and three lugs are set in near the cutting edge corresponding in size and distance apart to the holes in the blade of a Gillette safety razor. In setting these lugs care must be used to set them at such distance from the edge of the plane bit that when the razor blade is in place on the lugs its edge will project not more than a hair's breadth beyond the edge of the bit. If the razor blade projects further its cutting edge will not be sufficiently stiffened by the edge of the bit, and the elasticity of the blade will make it impossible to cut sections of uniform thickness. The blade is further stiffened and held in place by the "iron" or stiffener of the bit, which is regulated with a set screw to bring pressure about 1/16 inch from the edge. With the blade and the iron properly adjusted it is possible with the freezing microtome to cut sections 15 microns or even 10 microns in thickness.

The advantage of having a number of replacable blades of admirable keenness of edge, at an insignificant cost, will appeal strongly to anyone who has attempted to keep the old style heavy microtome knife in condition.

February 10, 1913.

TOXIC SPLIT PRODUCTS OF BACILLUS TYPHOSUS

JAMES W. JOBLING AND CARROLL G. BULL

Bacterial toxic substances are easily divided into different classes. In one we can put the true soluble toxins of bacillus diphtheriae, bacillus tetani, etc. These toxins are considered specific secretory products of certain bacterial cells, just as pepsin is a specific secretory product of certain animal cells. Animal organisms react to these toxins by producing specific counteracting bodies that neutralize the toxic bodies in definite multiple proportions, however high the multiple runs. The toxic substances of a second class of bacteria bear a very different relation to the bacterial bodies by which they are produced and the reaction products of inoculated animals are different from those produced by toxins of the first class. Bacillus typhosus, Bacillus coli, etc., produce toxins of this class. The relation of the toxic substances derivable from this second class of bacteria to the cells by which they are produced not being definitely determined, and the various immune sera produced by the whole bacteria or substances derived from them not having met with any marked success, the object of the present work was to learn more about the biological and chemical nature of such substances.

Bacillus typhosus was the organism selected for this study. The bacteria were grown on plain agar, washed free of adherent media, and suspended in physiological salt solution. Dogs were used as the experimental animals, and all injections were intravenous.

Experiment 1. Two c. c. of thick emulsion of typhoid bacteria were injected intravenously into a dog weighing ten pounds. Thirty minutes after the injection the animal became very sick and manifested, successively, vomiting, severe bloody diarrhea, signs of exhaustion, labored breathing, stupor and death. Autopsy:—bloody fluid in peritoneal cavity, mesenteric vessels engorged, visceral peritoneum rough and dull, subserosal hemorrhages scattered over small intestine, kidneys dark and congested, and the lumen of the small intestine contained much blood.

Experiment 2. The emulsion of bacteria was boiled for ten minutes and injected. The symptoms and autopsy were similar to those of experiment one.

Experiment 3. The bacteria were dissolved in an alkaline solution and neutralized previous to injection. Results were the same as those of experiments one and two.

These experiments show that typhoid bacteria do contain toxic substances and that such substances are not destroyed by heat or by solution in an alkali.

Experiment 4. The coagulable proteins of the bacterial emulsion were removed by heat and acid precipitation and the clear filtrate injected. No symptoms followed.

Experiment 5. The bacterial bodies were dissolved in an alkali previous to precipitation. The filtrate was non-toxic. Hence the toxic substances were removed from a fresh emulsion by heat and acid precipitation.

Experiment 6. An emulsion was digested for five days at 37° C., with leukoprotease and then precipitated by heat and acid. This filtrate was very toxic, one to three c.c. being fatal. The symptoms and pathology were similar to those of experiment 1.

Experiment 7. An emulsion was digested for three weeks and gave a non-toxic filtrate.

Thus digestion with leukoprotease changes the toxic substances from a coaguable to a non-coaguable state and continued digestion destroys it. A filtrate prepared as in experiment 6 was fractionated with amonium sulphate into half saturation precipitate, whole saturation precipitate, and non-precipitated fraction. The half saturation precipitate contained almost the total toxicity of the unfractionated filtrate.

SUMMARY:

1. A single intravenous infection of a sufficient number of freshly washed typhoid bacteria into dogs produces the symptoms and pathology which characterize anaphylaxis in these animals.

2. These results are not produced by the coagulable-protein-free filtrate from a fresh emulsion, while a similar filtrate from an emulsion digested with leukopro-

tease is very potent; the toxic portion of the bacterial bodies being changed from a coagulable to a non-coagulable state.

3. The symptoms and pathology described are not specific since they can be produced by substances other than typhoid toxins.

4. Digestion with leukoprotease furnishes a method of liberating toxic substances from typhoid bacteria which resembles the processes of nature more closely than the methods heretofore used.

5. The toxic substances thus liberated are not destroyed by a heat and acid precipitation of the coagulable proteins, and are of the nature of primary proteoses.

March 10, 1913.

FURTHER OBSERVATIONS ON THE RELATION OF FATS TO ANESTHESIA

EVARTS A. GRAHAM

(From the Otho S. A. Sprague Memorial Institute Laboratory of Clinical Research, Rush Medical College, Chicago.)

In 1910[1] it was shown by the author that the period of depression of phagocytosis which occurs during and following an ether anesthesia could be greatly shortened if fat were administered immediately after the anesthesia. In an earlier article[2] I also called attention to the fact that if such a fat as olive oil is given by mouth after the narcosis, many of the unpleasant (and at times serious) after-effects of anesthesia are prevented, notably nausea and vomiting. Since this time further experiments have been done both by myself and others bearing on this subject. Ferguson[3] has recently attacked the idea of preventing the post-anesthetic nausea by the administration of fat chiefly on theoretical grounds. His two principal assumptions, neither of which he sup-

1. "The Effects of Ether on Certain Processes of Immunity," Jour. Amer. Med. Assn., 1910, liv, 1043; "The Influence of Ether and Ether Anesthesia on Bacteriolysis, Agglutination and Phagocytosis," Jour. Infect. Dis., 1911, viii, 147.

2. "Olive Oil for Postanesthetic Nausea," Jour Amer. Med. Assn., 1909, liii, 2094.

3. "The Use of Olive Oil to Prevent or Relieve Postanesthetic Vomiting," N. Y. Med. Jour. 1912, xcv, 1359.

ports with experimental evidence, are: (1) that ether when taken by mouth will not cause vomiting sufficiently soon after its ingestion to support the idea that the local initiation of the gastric mucosa by excreted ether may be an important factor in post-anesthetic nausea and vomiting, and (2) that the administration by mouth of a fat following an anesthesia will carry down into the intestine any ether that may be in the stomach and hence allow it to be reabsorbed, constituting thus an actual disadvantage rather than an advantage. In addition he states that clinically the use of a fat for such a purpose has been followed by no better results than without it, although he fails to present any statistics.

On the contrary, the results here reported differ radically from Ferguson's theoretical conclusions. Experiments were conducted on nine pairs of dogs of approximately the same size in such a way that of each pair one dog was given by stomach tube ether shaken up with water and the other dog was given in the same way ether which had been shaken up with a fat emulsion. The amount of ether varied in different instances from 15 c.c. to 50 c.c. The amount of fat or water used in each case was approximately three times the amount of ether. Six of the dogs (or 66.6 per cent.) which received ether with water, but without fat, vomited profusely; and only one of those vomited which received the ether and fat mixture. The vomiting usually occurred almost immediately after introducing the ether. But far more striking were the differences observed in the general effects. In every case the dog which received only the ether and water showed much deeper narcosis than the one to which the fat was given; and this in spite of the fact that frequently a fairly large amount of the ether was thrown out in the vomitus. In several experiments the difference was so marked that the dog receiving the ether and water nearly died, while the dog which was given the same amount of ether shaken up with fat showed only a slight unsteadiness of gait.

These facts lead to the following conclusions: (1) That the introduction of ether into the stomach will cause vomiting so soon that the direct irritation of the gastric mucosa seems to be a factor. (2) That the giving of fat along with the ether serves not only to pre-

vent nausea and vomiting, but also inhibits the absorption of ether from the gastro-intestinal tract.

Of further interest is the fact that clinically the use of fat (olive oil) at our hands has seemed to diminish the amount of post-anesthetic vomiting very greatly. Thus out of 112 operative cases which received no fat after the anesthesia 60 per cent. vomited; and of 270 cases which were given fat only 23 per cent. vomited.

March 10, 1913.

AN ANAEROBIC, HEMOPHILIC DIPLOBACILLUS FROM THE ETHMOIDAL SINUS

VIRGIL H. MOON

A vast amount of work has been done on the bacteriology of accessory sinus diseases, and almost every bacterium which is pathogenic for the human species has been found associated with disease of the accessory sinuses. Yet the occasional discovery of an organism not elsewhere described shows that the field has not been exhaustively worked out, and that it offers promising opportunity for further study.

The organism here described was found associated with a chronic suppurative inflammation of low grade in the left ethmoidal sinus of a man past middle life. Examination of the mucopurulent discharge from the sinus showed many small Gram-negative diplobacilli occurring for the most part within the cells. These diplobacilli were slender with rather tapering ends, and tended to lie parallel rather than crosswise or at random. They were found constantly in the discharges examined at intervals for three months, and were the predominating organism, no other organism being found constantly nor in such numbers.

Attempts at cultivation by ordinary methods on ordinary media were uniformly unsuccessful. Even when plated out on human blood agar no colonies were visible which on examination gave an organism resembling the diplobacillus found in the discharge. However, better success resulted when a small quantity of the material was streaked across the surface of a blood agar plate or slant with a platinum loop or spreader. After

24 hours' incubation minute almost invisible dust-like colonies were seen scattered over the surface of the blood agar thus inoculated. These colonies when magnified 100 diameters appeared discrete, round, glistening, transparent and almost like dewdrops. When stained the organism was seen to have the same appearance as those found in the discharge, and presented the following characteristics: A pleomorphic diplobacillus sometimes so short as to resemble cocci in form, especially in young cultures; in older cultures it showed a marked tendency to form long threads. The average size of a single characteristic bacillus was 0.3 by 1.2 microns.

The organism is non-motile, shows no capsule, forms no spores, so far as observed, though often granules are seen resembling somewhat those of the diphtheria bacillus. It stains readily with the ordinary stains, is decolorized by Gram's method and is not acid fast. It grows best on human blood agar of alkaline reaction, grows fairly well on ordinary blood agar or broth prepared with sheep, goat or rabbit blood, but refuses to grow on Loeffler's medium or on any medium not containing hemoglobin.

The organism is anaerobic, though slightly facultative. It grows feebly for two or three days aerobically if transferred daily, but I have not succeeded in growing it longer if exposed to air, except in the presence of other organisms as diphtheria or pseudodiphtheria bacilli or staphylococci. In mixed culture with one of these organisms it grows abundantly aerobically, forms much larger colonies, may be transferred on blood medium indefinitely and seems to inhibit the other organisms so that the diplobacillus predominated in the symbiosis. This organism autolyses in normal salt solution readily if heated to 60 C. and more slowly at room or incubator temperature. It is non-pathogenic for rabbits and guinea-pigs even when injected intravenously in large quantities.

The patient who is host for this organism is a healthy, robust, well-nourished man and shows no general symptoms of infection. The condition is chronic, having lasted in its present form for four or five years. The patient is unable to recall definitely how the condition

began or whether it was preceded by an acute infection. The discharge is yellowish, muco-purulent and rather profuse in quantity, about 4 c.c. being discharged in an hour's time. The patient's serum agglutinates the organism at a dilution of 1:16, normal serum showing no agglutination. Opsonins for this organism are also present in considerable quantities. The opsonic index or ratio of phagocytosis of normal leukocytes in the presence of the patient's serum to that in the presence of normal serum is 3:1.

These facts, together with the constant occurrence of this organism in the leukocytes of the discharge from the sinus, give ground for the supposition that it is a pathogenic organism and the etiological factor in this case.

This bacillus may have been described by previous observers, but in an extended search of the literature, a description to which this organism corresponds has not yet been found. It conforms quite closely to the influenza bacillus in many details, but differs from it in the following particulars: It is larger than the influenza, grows as a diplobacillus, gives more involution forms, stains more readily, and is anaerobic, whereas the influenza bacillus is aerobic. Undoubtedly it belongs to the group of hemophilic organisms of which the influenza bacillus is the best known representative.

March 10, 1913.

THE PERMEABILITY OF THE TUBERCLE BACILLUS TO THE "FAT-DYES"

HOPE SHERMAN

In view of the almost universally accepted fact of the existence of a fatty or fat-like constituent of the tubercle bacillus, it seems reasonable to suppose that the bacilli might manifest a particular affinity for the so-called "fat dyes." Accordingly experiments were made to learn whether "fat-dyes" stain the tubercle bacillus or its ether extract, and, having done so, withstand decolorization with acid or alcohol, in the hope that the results might perhaps prove suggestive in the

attempts to develop a chemotherapy of tuberculosis. The fat-dyes used were the sudan series (sudan III, sudan yellow, and sudan brown), scarlet R, and Nile blue sulfate. Bismarck brown, indulin, indophenol blue, and dimethylaminoazobenzol, which are sometimes used for staining fats, were also tested, as well as basic fuchsin, eosin, neutral or anilin red, Janus green, and methylene blue, this last group falling quite outside the class of fat-dyes.

The results obtained are briefly as follows:

All the dyes used, whether fat-soluble or not, stain pure cultures of tubercle bacilli, *en masse*, because of the presence of stainable substances outside the bacilli.

Sudan III does not stain individual tubercle bacilli, either in smears or pure culture, in tuberculous pus, or in tuberculous tissue.

Sudan yellow and sudan brown stain the bacilli faintly in pure culture smears on prolonged exposure, or on heating.

Scarlet R resembles sudan III in behavior, but is slightly less inefficient.

Nile blue sulphate gives a faint and rather unsatisfactory bacillus-stain, as does Janus green, for the most part.

Indulin stains the bacilli faintly on prolonged application.

Indophenol blue does not stain the bacilli.

Dimethylaminoazobenzol gives a faint and unsatisfactory bacillus-stain.

Basic fuchsin, which is only slightly fat-soluble, eosin and methylene blue, which are not fat-soluble, stain the individual bacilli deeply in a relatively short time.

All the dyes used stained the impure ether extract of tubercle bacilli, while the purified ether extract was less readily stained by the majority of the dyes not classed as "fat-dyes."

The behavior of the dyes toward the impure ether extract corresponds with their behavior toward cultures of the bacilli, and is very different from that toward the individual bacilli. These facts indicate that masses of ether-soluble substance exist on the surfaces of cultures

as well as within the bacterial protoplasm, and it is with this extra-cellular material that the dyes combine.

Basic fuchsin and eosin, and to a less extent Bismarck brown, resemble the regular "fat-dyes" in the ease with which they stain the ether extract.

The "fat-dyes" are not serviceable for the detection of tubercle bacilli in pus or in tissue, nor for staining them in pure culture.

Experiments with crushed bacilli confirm Benian's view that the acid-fastness of the tubercle bacillus depends on the physical integrity of the bacterial cell.

The fatty constituents of the tubercle bacillus are not, *per se,* the cause of the staining reaction characteristic of this organism.

April 14, 1913.

ON RAPID PRODUCTION OF SPECIFIC PRECIPITINS

LUDVIG HEKTOEN

(From the Memorial Institute for Infectious Diseases, Chicago.)

The method of Fornet and Müller, Borhoff and Tsuzuki, and Gay and Fitzgerald[1] has been followed in the immunization of rabbits with the serum of various species. According to this method the serum is injected in increasing doses on three successive days, and usually intraperitoneally, the rabbit being bled on the twelfth day after the last injection. The results obtained are in good agreement with those of the investigators mentioned. Rabbits thus injected with dog, horse, sheep, swine, beef, chicken or human serum, usually in doses of 5, 10 and 15 c.c., yielded precipitins in sufficient concentration to cause precipitation in dilutions of the corresponding antigenic serum of from 1 to 1,000 to 1 to 20,000, and sometimes even in higher dilutions. Considerable individual variation in the power to produce specific precipitins was observed, but this variation probably is no greater when this rapid method is used than with the older method of injection of the antigen

1. An improved rapid method of producing precipitins and hemolysins, Univ. Cal. Pub. in Pathology, 1912, ii, 77.

at longer intervals. When the course of the development of specific precipitin in the blood is followed by daily tests, a curve is obtained that corresponds to the simple antibody curve, the acme occurring about the twelfth day. The first demonstrable increase in precipitin usually takes place rather suddenly during the third or fourth day after the last injection; there now ensues a gradual rise until the acme is reached after which comes a gradual decline.

April 14, 1913.

A CASE OF ACROMEGALY WITH POLYGLANDULAR SYNDROME

FRANK K. BARTLETT

(From the Department of Pathology of the University of Chicago.)

There are many well-known polyglandular syndromes, depending on the ablation, the hyposecretion, the hypersecretion, or the perverted secretion of certain glands of internal secretion. Prominent among these is acromegaly, due to an hypertrophy of the anterior lobe of the hypophysis. Acromegaly or adult gigantism has never been produced experimentally in animals. It is usually accompanied by a polyglandular disturbance involving one or more of the glands of internal secretion besides the hypophysis.

Erdheim, Benda, Lewis, Fischer, Cushing and others have shown that not only is there an hypertrophy of the anterior lobe of the hypophysis in acromegaly, but that there is an hyperplasia of the acidophil type of chromophil cell of the anterior lobe. A number of other theories on acromegaly are prevalent, but do not give satisfactory explanations to all of the facts as does the above hypothesis.

From birth on the chromophil cells of the anterior lobe increase in number until at middle age they are equal to the chromophobe cells; from middle age on, the chromophil cells decrease, so that by old age the same relationship between the chromophobe and the chromophil cells exists, as is found at birth. Physiologically there is hypertrophy of the chromophil cells

during puberty, pregnancy and the climacteric. Pathologically these cells are reported to increase during long, acute illnesses, after pancreasectomy, after thyroidectomy and after castration. Cushing and others have shown that if hypertrophy of the anterior lobe occurs before puberty, gigantism results, but if hypertrophy occurs much later than puberty, after there is ossification of the epiphyses of the long bones, then acromegaly results. Acromegaly is then the adult manifestation of gigantism. One is quite justified in concluding from the light of recent experimental and clinical investigations, that bone growth is governed to a large extent, if not entirely, by the anterior lobe of the hypophysis.

It would seem that feeding or injection of the desiccated gland or of its extracts, would produce gigantism in puppies and some acral change in adult animals; almost the reverse has been true. The injection and feeding experiments of Caselli, Cushing, Parisot and others have resulted in an underdevelopment of the skeleton, and a stunting, rather than an overgrowth of the bones and tissues of the body.

In the large porportion of cases of acromegaly, symptoms of hyposecretion of the anterior and of the posterior lobe soon develop. In the posterior lobe this is due to pressure atrophy, while in the anterior lobe where the struma has grown, it is due to degenerative processes in the cellular elements (namely, regions of cystic necrosis and of hemorrhage) and presumably to a disappearance of the acidophil granules in the chromophil cells leaving the so-called chromophobe strumas. These chromophobe strumas have been mistaken for sarcomas; they are in fact quite different from sarcomas in so far as their course is longer, they do not produce metastases nor infiltrate the surrounding tissues, and mitotic figures are more infrequent.

The following case of acromegaly with polyglandular syndrome was a patient in the service of Dr. C. H. Lovewell through whose kind permission an autopsy was allowed. Dr. H. Gideon Wells performed the autopsy.

Clinical History.—The patient was 25 years of age at the time of his death. His parents state that he was always a

queer boy. About one year before his death he first noticed that his hands were getting larger. Six months later he began to lose sexual desire, and still two months later he became impotent. At about this time he had occasional severe headaches. Polyuria was marked, as was diaphoresis, especially at night. One month before death headaches increased in frequency; his eyesight at this time was becoming foggy, especially that of the right eye. Several months before death irritableness, moodiness and forgetfulness were plainly noticeable by his wife and by the man for whom he worked as a driver. On Nov. 13, he was compelled to quit work because of a frightful headache. He was conscious until the evening of November 18; he died on November 19, at 4 a. m. It is thought by his wife that possibly he became a little heavier during the last few months prior to his death.

Autopsy Report.—The body is not fat, the weight being approximately 160 pounds. The height is 6 feet and 3 inches. The texture of the skin is normal. The face is large but no part is prominent. The hands are considerably enlarged, the enlargement being transverse and the thickening seemingly more fibrous than bony. The left forefinger measures 75 mm. about the middle joint, which is 10 mm. more than normal for a man of his build. Each hand around the knuckles measures 211 mm. There is no apparent enlargement of the feet. The superficial lymph-glands are all slightly enlarged. The costochondral junctions of the ribs are not swollen.

The abdominal and thoracic cavities are without significant alterations. The thyroid gland is about twice its normal size and weighs 65 grams. It contains a large amount of colloid which is distributed evenly throughout. Two accessory thyroid glandules are present. The thymus is persistent, well defined from the surrounding tissue by a thin fibrous capsule. It is fetal in macroscopic appearance of the cut surface. Two small accessory thymus glands are found just beneath the right lobe of the thyroid. The weight of the thymus is 22 grams.

The spleen is noticeably enlarged and soft, as are the liver and kidneys. All the lymph-glands of the body are enlarged, especially those of the mesentery and mediastinum; these are somewhat soft and on cut section are pearly gray in color.

The adrenals are of normal size and appearance.

The heart, blood-vessels, trachea, lungs, esophagus and stomach are all of normal appearance. The small intestines are filled with fluid; Peyers patches are slightly hypertrophied. The prostate, urinary bladder and ureters are normal. The testicles, unfortunately, were not obtained.

The skull is exceptionally thin and soft. The sutures give the impression of not having fully united. The brain is dry, swollen and pressed somewhat down into the foramen magnum on account of the increased cranial pressure and the swelling of the brain. The convolutions are broad and flat, while the sulci are shallow and narrow. The sella turcica is enlarged to 2.5x2x2 cm. It is tensely filled by a light chocolate-brown colored tumor which extends upwards, destroying the infundibulum, and forewards so that it pushes the optic chiasma before it, flattening the right side more than the left. Outside of the sella turcica the tumor is of a coarsely granular and spongy nature.

The pineal body protrudes conspicuously from underneath the corpus callosum. It is 13x6x5 mm. in size, weighs 940 mg., and is approximately two and one-half times as large as normal.

Microscopical Examination.—The thyroid gland represents a colloid goiter with marked desquamation of the parenchymatous cells into the alveoli.

The parathyroids are of normal size and microscopic appearance. The same may be said of the carotid glands, one of which was obtained.

The thymus is typically similar to that of an infant. Hassel's corpuscles are large and contain considerable débris in their centers. The capsule is very thin. There is no fibrosis or any sign of involution. The accessory thymuses are of similar appearance.

The adrenal is noticeably changed in that the zona fasciculata is abnormally vacuoled, and the chromaffin cells of the medulla are increased in number and size, extending in some places through the cortical layer almost to the capsule.

All the lymph glands examined, as well as the spleen, show a marked proliferation of the large endothelial cells, outside of the germinal follicles as well as within them. The lymphoid patches in the intestines present a similar picture.

Both the liver and kidneys present a slight connective tissue hyperplasia and to some extent a swelling and granular condition of the parenchyma.

About the entire periphery of the pineal gland is a border of cells, resembling epithelioid cells, arranged mostly in bunches and strings, but often assuming the arrangement of alveoli with lumena of an indefinite nature. In places this cellular border is 3 mm. in thickness. Running in from the connective tissue capsule are the numerous connective tissue trabeculae dividing the glandular periphery into numerous compartments, filled with the typical parenchymatous cell of the pineal body.

The nuclei of these cells average 13 microns in diameter; they are oval, vesicular and contain a fairly definite nucleolus, not always distinguishable from small groups of chromatin material. No pigment or granules of a secretory nature can be seen. Psammomata are lodged in small numbers at the inner edge of the peripheral border.

The hypophyseal tumor is composed of masses of oval or round cells, with a well-defined cytoplasmic border. The nuclei are either oval or round and are deeply stained with hematoxylin, indicating an abundance of chromatin material. Their general arrangement is alveolar, though this is somewhat ill defined in places. Mitotic figures are infrequent. With Van Gieson's stain there are seen delicate strands of connective tissue here and there, in which run blood capillaries. Compared to the normal hypophysis, the blood supply and connective tissue content is scanty. The whole mass is permeated with diffuse hemorrhages and small regions of diffuse necrosis. With special granule stains (acid fuchsin methylene green), the nature of the cells composing this tumor are found to be of the acidophil type of chromophil cell of the anterior lobe.

The posterior lobe of the hypophysis could not be found.

Unfortunately the testicles were not obtained, but from the clinical history and from the findings of similar cases, one can conclude with almost certainty that the cells of Sertoli and perhaps the cells of Leydig are atrophied.

Summing up, this case presents the polyglandular syndrome of (1) a chromophil cell adenoma of the anterior lobe of the hypophysis; (2) a persistent and non-involuted thymus; (3) a colloid goiter with marked desquamation of the parenchymatous cells; (4) hypertrophy of the chromaffin cells of the adrenal medulla; (5) hyperplasia of the endothelial cells of the lymph glands and of the spleen; (6) enlargement of the pineal body and presumably (7) atrophy of the cells of Sertoli and of Leydig in the testes.

Attention may be called to the fact here that polyglandular disturbance no doubt had been present for at least ten years, since in the thymus, which normally atrophies at about the age of 13 (Hammar), there is no evidence of fibrosis or other change indicative of involution.

April 14, 1913.

STUDIES ON THE TRANSMUTATION OF PNEUMOCOCCI AND STREPTOCOCCI

E. C. ROSENOW

(From the Memorial Institute for Infectious Diseases, Chicago.)

The morphologic and biologic characteristics of the organisms were studied in conjunction with the pathogenic powers. All the recognized methods for the differentiations of streptococci and pneumococci were employed. The strains were obtained from various sources. All were plated on blood agar at least twice and single colonies used for the inoculations. In order to exclude the possibility of mixed cultures three strains of hemolytic streptococcus, six of streptococcus viridans, two of pneumococcus and two of streptococcus mucosus were obtained from single organisms. The "pure-line" strains behaved essentially as those obtained by the plate method.

In previous papers I have shown that the streptococcus viridans can by animal passage be made to take on the characters of typical pneumococci. This has now been done in each of seventeen strains. It seems, therefore, that streptococcus viridans is a much attenuated modified pneumococcus and I have reported studies on cases of subacute or chronic infectious endocarditis as "chronic pneumococcus endocarditis."

By appropriate means I have been able to convert fourteen strains of typical hemolytic streptococcus into streptococcus viridans. After this transformation had taken place the affinity for the joints of the organisms as hemolytic streptococci disappeared and just as in other strains of streptococcus viridans the affinity for the endocardium became apparent. It therefore seemed that these strains just as other strains of streptococcus viridans could by animal passage be converted into pneumococci. This was found actually to be the case. Two of these strains were converted into typical pneumococcus and one into streptococcus mucosus as well. Nine strains of pneumococci and five strains of streptococcus mucosus have been converted into hemolytic streptococci. Three strains of "micrococcus rheumaticus" have been converted into typical pneumococci, four into hemolytic streptococci and one into strepto-

coccus viridans, hemolytic streptococcus and pneumococcus. For the complete transformation of streptococci into pneumococci animal passage has thus far been found necessary. The transformation is gradual and it takes from eight to twenty-five animal passages. Subcutaneous, intraperitoneal and pleural injections make for greater changes than intravenous injections. In this series six strains which had been converted into pneumococci, two of which were originally hemolytic streptococci, one streptococcus mucosus and three micrococcus rheumaticus were selected and studied intensively to determine whether they were really pneumococci. All were at one time typical lanceolate, encapsulated diplococci indistinguishable morphologically from known pneumococci. All fermented inulin, none precipitated serum glucose agar, all produced green colonies on blood-agar plates and acid when grown in pneumonic serum. All were soluble in bile and autolyzed in NaCl solution under ether. They grew quite readily in streptococcus broth culture filtrates but not in pneumococcus (Marmorek's test) behaving like other pneumococci in this respect. All were highly virulent to animals (rabbits, guinea-pigs, white rats and mice), killing each by rapidly fatal pneumococcemia. Rabbits were immunized with one strain as a hemolytic streptococcus and the same strain as a pneumococcus. The former gave rise to the formation of specific antibodies (opsonin) to the homologous and other streptococci while the latter gave rise to a specific increase in opsonin to the homologous and other pneumococci. The transformation seemed complete. During the intermediate stages the acquired properties tend to disappear and the organism may revert to what it was originally, but after the transformation is complete the acquired properties become quite fixed, and the strains now behave quite as do those which are obtained from the usual sources. In order to change the characteristics it is necessary to place these organisms under stress or strain. This seems to call forth latent energies which do not manifest themselves under ordinary conditions. Of the many ways that have been tried to bring about important changes the growth in symbiosis with other bacteria, especially *B. subtilis*, on blood-agar plates, and growth

under varying degrees of oxygen tension and variations in salt concentration proved most effective. When hemolytic streptococci are grown under relatively low oxygen tension their hemolysing power is maintained, when grown in pure oxygen they lose this property gradually and become green producing streptococcus viridans. This fact would seem to explain why streptococcus viridans predominate on the surface of normal or only moderately diseased tonsils and other mucous membranes when at the same time the crypts harbor hemolytic streptococci in predominating numbers.

April 12, 1913.

The details of these experiments will appear in a forthcoming number of the Journal of Infectious Diseases.

ON ANAEROBIC ORGANISMS ASSOCIATED WITH ACUTE RHINITIS

RUTH TUNNICLIFF

(From the Memorial Institute of Infectious Diseases, Chicago.)

A large amount of work has been done to determine the cause of acute rhinitis, but so far as I have been able to determine all the investigations have been made with aerobic methods.

The organism now described has been found during the early stages of acute coryza, while the discharge is mucoid in character. At this time few, often no other bacteria are present in the smears. The organism is often found in large numbers. As the mucus disappears or the discharge becomes purulent, it decreases in number and finally disappears. It has been observed in all of the cases of acute rhinitis studied. Eighteen different persons have been examined during the acute attack, one during each of four attacks and another during each of five, so altogether, I have made observations during twenty-five distinct attacks. Many examinations were made during the course of the infection in nine of these cases. In case of an accompanying pharyngitis, tonsillitis or bronchitis, the organism is also found, sometimes in very large numbers. It was present in small numbers in five cases examined when the rhinitis was disappearing. It was not found in thirteen normal per-

sons, in one case of suspected syphilis and one case of diphtheria. Only in one normal person a few were observed. These same organisms have been seen in three cases of chronic rhinitis and isolated in pure culture once by Dr. Geo. F. Dick. In order to find the organisms a fair amount of mucus should be spread on a slide and often a large number of fields must be examined. They generally appear in clumps, but may be found separate.

It stains best with carbolgentian-violet and carbol-fuchsin but stains rather faintly even with these stains. It does not stain by Gram's method, methylene-blue, thionin or the Giemsa stain. It may be seen by dark field illumination. Some of the organisms seem to be flexible and possibly move a little, but most of them appear immobile, which might be due to the large amount of mucus present. The organisms vary from 5 to 8 microns in length and from one-third to one-half in width. The ends are pointed or slightly rounded. Generally the organisms are slightly curved but may be straight, wavy or bent over at one end. Sometimes an enlargement in the form of a ball is seen at one end. The organisms are sometimes arranged in bunches, several radiating from a central mass. Sometimes a ring is attached to one extremity.

The organism is a strict anaerobe and grows slowly, at least at first. I have isolated them in pure culture four times, twice from the nose, twice from the throat. They were isolated on goat blood agar, the agar being slightly alkaline. The colonies appear in from five days to a month as small round dull growths. After several transfers growth becomes more active. In old cultures the growth becomes thick and greenish yellow in color. The organisms grow on dextrose agar, ascites agar, and ascites agar with rabbit kidney tissue. They produce a definite growth along the stab canal but no haziness. They grow a little on plain agar. They produce a flocculent growth in dextrose broth.

The organisms possess slight motility but lose it quickly. Attached to the ends and sides and also free are light refractile bodies, the free bodies being very motile.

In cultures the organism measures from 3 to 8 microns in length and one-third to one micron in width. It now stains a little more deeply with carbol-gentian-violet than in the smears from mucus, but remains Gram-negative. Those grown on dextrose-agar show deeply staining bands.

Morphologically they look like the organisms found in the smears from the mucus. After long cultivation some strains have a tendency to become larger, straighter and less bunched. In the early cultures they appear delicate, straight, slightly curved, some quite wavy. Some show a radiating arrangement. Darkly staining bodies are seen attached to the ends and sides and also free. An organism with a ring at one end is occasionally seen. Morphologically the organism looks like a spirochete, but culturally it seems more like a bacillus, and whether it is a spirochete or a bacillus must be decided later.

During the acute stage of the rhinitis the opsonic index to this organism is low, rising as the infection subsides.

A slight rhinitis has been produced three times in human subjects (twice in myself, once in a laboratory assistant) by swabbing the nose with a pure culture of this organism. A pharyngitis also occurred twice. The infection began from six to eight hours after the inoculation and lasted about forty-eight hours. The organisms were present in fairly large numbers in the nose and pharynx (in the cases with pharyngitis) eighteen hours after the inoculation. They could still be found for about three days. They were not present before the inoculation. The opsonic index was taken during two of these infections. Both times it fell below normal, rising above normal as the infection disappeared.

A slight rhinitis has been produced in a dog also, the organisms disappearing from its nose 24 hours after inoculation.

Whether this anaerobe is the cause of acute rhinitis must be determined by further investigation. My observations show that in the cases of acute rhinitis examined, it was present constantly during the early stage of the coryza and disappeared as the infection subsided.

May 12, 1913.

PYRUVIC ACID AND ACETOLE IN THE DIABETIC ORGANISM

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A normal organism utilizes sugar. Utilization of sugar consists chiefly of three things: namely, oxidation, reduction (fat formation), polymerization (glycogen formation). There are doubtless other reactions into which sugar can enter, but these are the chief ones.

In diabetes (by which we here mean pancreas diabetes, or diabetes mellitus), the body loses, in part at least, its ability to utilize sugar. In the severest cases, 100 grams of sugar fed by mouth, may lead to the appearance of 100 grams of extra sugar in the urine. *This 100 grams of sugar must have* escaped burning! It cannot have been converted into fat and subsequently reconverted into sugar, because we have no proof that fat once formed can be reconverted into sugar in any considerable amount. It may, to be sure, have been stored for a moment as glycogen, and then reconverted into sugar, but this also is unlikely, because there are many experiments which indicate that in diabetes the liver and muscles actually lose in a considerable measure their power to build glycogen from sugar.

Why does the diabetic body fail to do with sugar any of those things which a normal body does?

Some have said, because two of the three things are dependent for their occurrence on the preliminary occurrence of the other one so that when one fails, the other two necessarily follow suit. Thus Naunyn and the Von Noorden school look upon glycogen formation as a necessary prelude to the further utilization of sugar. Others have held that there is a primary inability to oxidize sugar and that the other disturbances are secondary to this. Again others have laid the trouble to other sources. We have entertained the theory that all utilization of sugar demands a preliminary activation or dissociation of the glucose molecule, and that glycogen formation, oxidation, and fat formation, will none

of them occur normally unless the dissociation is adequate. This view is similar to the one expressed by Schultzen in 1871.

Now it is interesting to note that while a glucose molecule may be entirely unavailable for use in a completely diabetic body, this is not true in the same degree for certain substances which are chemically very closely allied to glucose. Thus gluconic acid seems to be capable of oxidation in the diabetic body, although it differs to only a very slight degree from glucose. This suggests that only one step, perhaps the first in the breakdown of a glucose molecule, is the one which a diabetic cannot execute. And if this is the case, it might be thought possible to perform this step in the laboratory and administer to the patient his carbohydrate in *premetabolized* form.

What is the first step in the breakdown of a glucose molecule? What are the subsequent steps? Which one, or which ones fail to occur in diabetes? These are all questions which as yet have not been satisfactorily answered. An important problem is: (1) To find out how sugar breaks down in a body under normal circumstances; (2) to find out where the failure occurs in diabetes. These points when settled open the way to the study of deeper physiologic questions—questions intimately connected with the whole subject of internal secretions, the "correlations of the ductless glands" and their therapeutic control.

Thanks to the work of organic chemists, notably Nef, Wohl, Neuberg, Lobry de Bruyn and Emil Fisher, we know something of the way in which sugars break down outside the body, and of the intermediates which are thus formed *in vitro*. We, along with many others, have prepared certain of these intermediate products and subjected them to biologic tests, in healthy and diabetic animals, and in men. The logic is this: If a substance (A) is intermediate in the bodily breakdown of sugar, then if we make this substance in the laboratory and feed it to diabetics, the effect should have certain negative characters and certain positive characters; that is, if the intermediate is not too far down in the scale of sugar breakdown products, it should retain certain

characteristic biologic properties of sugar, but even if it does not show these, it should not produce any effects incompatible with the idea that this substance is constantly being formed in health, from the regular, normal breakdown of sugar. We have worked with a very considerable number of intermediates which occur in the breakdown of sugar outside the body. The two here under discussion are pyruvic acid and acetole.

PYRUVIC ACID, $CH_3CO.COOH$.

Pyruvic acid is formed *outside* the body during the destructive breakdown of glucose under certain circumstances. These circumstances are not such as would suggest pyruvic acid as a likely intermediate in the *normal* breakdown of sugar in the body, but it has been so held by Embden and his pupils and others because they believe that lactic acid, $CH_3CHOH.COOH$, is a regular normal oxidation product of glucose. If this were true it would be easy to see how lactic acid would yield pyruvic acid by alpha oxidation. This view has been adopted by Ida Smedley and others. Considerable polemic has also arisen as to whether pyruvic acid is capable of being reconverted into sugar in the diabetic body. Embden, Parnas, Baer and Ringer in New York have all worked with it.

Our experiments with this substance were carried out in January of this year. The work was done with dogs, made fully diabetic with phlorhizin, and in one case of human diabetes. When dogs are fully phlorhizinized and simultaneously fasted, they lose all the glycogen of the body, so that post mortem analysis shows no trace in the liver or muscles. It takes some time to take the glycogen all out of a dog, but when it is gone we can tell this by the fact that the sugar in the urine comes to bear a constant ratio to the nitrogen in the urine. It not only bears a constant ratio, but a ratio very close to the absolute figures 3.65 of glucose, to 1 of nitrogen. There is no special significance, of course, in striking a ratio of 3.65 to 1 unless it is a constant ratio and unless it occurs under certain carefully controlled conditions, when no food is being given, or when the food consists solely of fat and carbohydrate free protein, and in passing, it may

be well to remark that all meat, unless taken from specially prepared animals, has some carbohydrate in it. But when the ratio occurs under proper circumstances, it means that no glycogen is left in the body and that all or virtually all sugar in the urine is coming from body protein[1] (Lusk). Hence the constant relationship between the nitrogen and the sugar, since both represent fragments of the same protein molecules,—a torso and a head, as it were, both coming from the same body.

If to a dog in such a state, any substance is given which can be converted in the body into sugar, this sugar must appear in the urine, and since it will not cause the appearance of any additional nitrogen the D:N ratio will rise. We can then tell exactly how much extra sugar has been formed: i. e., how much sugar appears in the urine over and above that represented by the nitrogen times 3.65.

After giving ten and twenty grams of the sodium salt of pyruvic acid, we find each time a little extra sugar in the urine, a slight rise in the D:N ratio, but not much. Some of the pyruvic acid is actually reduced back into sugar. Since lactic acid, when administered in a similar manner, is converted quantitatively into sugar, it is easy to see how pyruvic acid by conversion back into lactic acid might yield some sugar. But this represents only some 10 per cent. of the total quantity and there are other things which indicate that the remaining 90 per cent. of the pyruvic acid goes in a different direction. Outside the body pyruvic acid splits very easily into acetaldehyde, $CH_3COH + CO_2$. Now, acetaldehyde in the body is capable of conversion into aldole (beta-hydroxy-butyric aldehyde) and this substance is capable of yielding beta-hydroxy-butyric acid and this aceto-acetic acid, and this acetone. Consequently, when acetaldehyde is given to a diabetic dog, it may cause an increase in the acetone excretion in the urine by this roundabout mechanism. Consequently if pyruvic acid split into acetaldehyde in the body we

1. Certain fatty acids (e. g., propionic) may yield some sugar (Ringer) but feedings of fat cause no rise other than that due to their glycerin. Probably the sugar-forming fatty acids do not occur in the breakdown of the fats to any extent.

might expect it to cause an increase in the output of the acetone bodies in the urine. Reference to the charts show that pyruvic acid actually causes an increase of the acetone bodies in the urine. Sugars are notorious for their characteristic ability to reduce the quantity of acetone bodies in the urine. Pyruvic acid does the reverse. This is incompatible with the idea that pyruvic acid can constantly be formed in the *normal* breakdown of sugars. Consequently we regard pyruvic acid as an abnormal breakdown product of sugar in the body, in agreement with Baer and Parnas. Our findings closely parallel those of Ringer in New York (as yet unpublished and personally communicated).

ACETOLE, $CH_3CO.CH_2OH$

Acetole is probably formed when sugars are heated with alkali outside the body. Walter Löb has suggested that it is an intermediate of the breakdown of sugars in the body, and as for pyruvic acid, his view has been given indorsement by many writers. Acetole is a substance which it is difficult to prepare and there are no published records of any biologic experiment made with this substance. Nef and Denis have perfected a method for preparing it. It is still a difficult preparation. Dr. Witzmann in our laboratory, made us a supply of this substance by following Nef's method. The charts show the results of our experiments with this material in phlorhizinized dogs. This work is thought to be the first which has been done with acetole along biologic lines.

When given in moderate quantities to healthy animals, it has caused some albuminuria and a considerable excretion of hemoglobin. When given to phlorhizinized dogs, we notice first an increase in the quantity of reducing substance in the urine, and a consequent increase of the D:N ratio. But we were able to prove that this extra reducing substance was not glucose. There was no corresponding increase of dextro-rotatory substance in the urine, and by distilling the urine, it was found that the extra reducing substance was volatile, and furthermore gave all the characteristic reactions of acetole. There appears to have been also a

slight increase in the quantity of acetone bodies in the urine.

Acetole acts, then, as an incompletely oxidizable substance, which is quite toxic for the kidneys, which causes no extra sugar to appear in the urine, but reacts in general as though it split so far as it splits at all into

$$CH_3COH + CH_2OH$$

(acetaldehyde and oxymethylene). The only other cleavage which could occur to acetole in the body would be a splitting as follows:

$$CH_2 + HCO$$
$$CH_2OH$$

(methylene and glycol aldehyde). If this occurred the right hand fragment (glycol aldehyde) would be capable of conversion into glucose. So that acetole would in this case cause extra sugar to appear in the urine. It does not do so. (P. Meyer.) Acetole, then, for the same reasons that have been assigned for pyruvic acid, is not a substance which qualifies either positively or negatively for a chief intermediate in the breakdown of glucose. We accordingly hold that Löb's hypothesis, in so far as it concerns acetole, is without positive experimental support.

May 12, 1913.

Note.—The experimental data will be published shortly in the Journal of Biological Chemistry.

CYCLOPEAN MONSTER

HARRY JACKSON

(From the Department of Pathology, Northwestern University Medical School, Chicago.)

A cyclopean monster is an anomaly of embryonal development in which the eyes are more or less fused and lie in a single orbital cavity in the median line of the face. These anomalies are not uncommon among the lower animals, especially the pig, but its occurrence in man is rare. The case herewith reported is the second I have seen within a period of two years; the first occurred in my hospital practice and was reported in

the *Journal of the American Medical Association*.[1] For the second case I am indebted to Dr. DeLee of the Chicago Lying-in Dispensary, and to Professor Zeit, who has kindly asked me to report it.

The etiology of the cyclopic defect is unknown. St. Hilaire[2] was the first to accurately describe it, and since his time many theories have been advanced to explain it. An early theory was that increased intrauterine pressure caused a fusion of the eyes. With increased knowledge of the embryologic development of the head, the fusion theory lost favor and the germinal theory was advanced. According to this theory, any injury or disease that causes a lesion of the early cerebral vesicle before the fifth week may so injure or destroy those anlage that normally go to form that portion of the face between the eyes, that they develop very little or not at all. This theory allows for all the gradations of cyclopic defect. Camille Dareste[3] was the first to produce these lesions experimentally and he showed that when the anlage for the nose were injured they failed to grow down between the eyes. Later, Spemann[4] ligated the eggs of certain fishes in the two-cell stage, placing the ligature obliquely to the first line of cleavage and repeatedly produced monsters with cyclopic defect. Stockard[5] produced the same result by growing fertilized eggs in a solution containing a trace of magnesium chlorid. As I have shown in my former article, there is very little support for the theory that cyclopean defects represent a reversion to an early stage in the phylogenetic development of man. The careful and minute study of the brains of these anomalies has been neglected till very recently. They afford excellent opportunity to the student of comparative anatomy and embryology for light upon many moot points in the development and physiology of the human brain. Nägeli[6] was the first to take advantage of such an opportunity and his report was unique until Black, under the direction of

1. Journal A. M. A., Oct. 30, 1909, p. 1483.
2. St. Hilaire: Traité de Tèratologie, Paris, 1832.
3. Dareste: Researches on the Artificial Production of Monsters, Paris, 1891.
4. Spemann: Zool. Jahrb. Suppl., 1904, vii, 429.
5. Stockard: Jour. Exper. Zool., 1907, iv, 2.
6. Nägeli: Arch. f. Entwick-mech. Bd. 5, H. 1, 1897.

Professor Herrick of the Department of Anatomy of the University of Chicago, undertook the study of the brain of my first case, the report of which will appear shortly.

History.—The specimen is that of a seven months fetus which was born dead. There is nothing obtainable in the history of the mother that points to intra-uterine trauma or disease.

External Examination.—The skin is macerated and the body is normally developed except for certain malformations of the face and arms. Above the well-formed mouth in which the tongue is visible, there is a double eye which is more or less fused. The nose is entirely absent from its normal location. Above the eye there is a snout-like projection.

The eye is situated in a palpebral fissure, rhomboidal in outline. The four sides of the rhomboid are formed by the union of the upper and lower eyelids meeting in the median line of the face. The palpebral fissure measures 3 cm. in width and 1.8 cm. in height. Within this fissure are two well-developed eyeballs which fuse in the median line. The pupils are oval in outline, the long axis parallel to the length of the body. The eyelids are well formed and bear eyelashes. Separate eyebrows are present. The optic cavity is a single large cavity and contains an opening in its center and posteriorly for the optic nerve. One-half centimeter above the eyeballs in the median line is a snout-like projection measuring $2 \times 1\frac{1}{4} \times 1\frac{1}{2}$ cm. At its extremity is a depression containing a pinpoint opening which leads into its interior. The ears are not fully developed and show seven distinct lobules to tragus and anti-tragus. Among other external signs are some malformations of the hands, which are bent backward at the wrist and twisted so that the fingers are in contact with the region of the elbow.

Internal Examination.—On removing the scalp, a large amount of reddish gelatinous material was found on the calvarium, and measured .5 cm. in thickness. On opening the skull, similar gelatinous material was found beneath the dura mater. The dura measured 2 mm. in thickness and was opaque; the sinuses were greatly dilated and filled with clotted blood. In the brain there was a large cyst measuring 5×3 cm. and situated in the region of the third ventricle. This also contained a gelatinous material similar to that described above. The brain itself was in a very poor state of preservation. It was red and soft and friable and weighed 98 gms. The cerebral lobes could still be distinguished but

their convolutions were flattened and not well defined. The cerebellum was present and all the cranial nerves were found with the exception of the olfactory nerves. No trace of these was discernible. The optic chiasma was not to be found but the optic nerve arose from the base of the brain in the median line as a double nerve and ran directly forward for a distance of 2 cm., dividing into two divisions just before it entered the eyeballs. From a posterior dissection of the eyeballs, it was seen that they were closely bound together by bands of connective tissue and fat. The selerae were continuous with each other but otherwise the development of each eye appeared to be distinct. A section of the proboscis, which, according to Treves, represents the anlage for the naso-frontal process, disclosed a hollow cylindrical organ at the base of which and in its walls were bone and cartilage; the hollow portion was filled with a thin gelatinous substance.

On median section of the body, the tissues were seen to be soft and red. The pleural cavities each contained 15 c.c. of a thick reddish fluid. The lungs were atelectatic and there were many adhesions of the pleurae to the diaphragm. The abdominal cavity contained 10 c.c. of reddish fluid and there were many dense adhesions of all the abdominal organs in contact with the diaphragm. The right lung weighed 13.5 gm., the left 12 gm. They were of a dark red color, solid, and airless. The surface was smooth, with dot-like grayish thickenings of the pleurae scattered here and there. On cut section, the tissue appeared homogeneous, solid and reddish. A reddish, purulent fluid could be squeezed from the bronchi. The thymus weighed 4 gm. and measured 5 x 2½ x 1 cm. It appeared as two flattened lobes covering the two auricles of the heart and adherent to the pericardium. The heart weighed 36.7 gm. and was about six times as large as the fist of the fetus. It easily filled two-thirds of the thoracic cavity. It measured 5 cm. in its broadest diameter and 5½ cm. from base to apex. The pericardium was somewhat thickened but free, and contained no fluid. The left auricle was greatly dilated, measuring 3 x 1½ cm., and filled with clotted blood. The right auricle was small and empty. The cavity of the right ventricle was large and empty; its wall measured 2 mm. in thickness. The left ventricle had a small cavity and its wall measured 5 mm. The foramen ovale was patent. The valves appeared negative.

In the abdomen, the stomach, pancreas, liver, spleen and kidneys were adherent to the diaphragm. Among the abnormal findings, the right kidney was seen to be markedly atrophic, and on cut section no kidney tissue was recognizable.

It weighed 2 gm. compared to 15 gm., weight of the left kidney. The liver showed a number of dense reddened areas in the right lobe, each the size of a small hazelnut. Its weight was 54 gm. The appendix appeared as a prolongation of the cecum and measured 4 cm. in length, and was coiled like the small intestine. The osteo-chondral junction of the lower end of the femur appeared normal.

The genitalia appeared normal.

There was a hemorrhage into the umbilical cord at the navel measuring 3 x 2 cm. Microscopic examination of the various organs and tissues revealed nothing definite as the tissues had undergone much marked post-mortem change.

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NUCLEOPROTEINS AS ANTIGENS *

H. GIDEON WELLS

The conclusion which seems warranted by the facts, elicited from the literature and by experiment, is that pure nucleins are probably not antigenic, at least not in the ordinary sense of the term, since neither of their constituents (nucleic acid and histones, or protamines) is antigenic. Therefore any antigenic property observed with preparations of "nucleoproteins" depends on the more or less adventitious proteins present in the preparations used in the experiments. There is no reason for believing that these protein-nuclein complexes represent a complex which exists in the cells, or that the proteins therein are in any particular degree specific or characteristic, either of the cells from which they come or of the nucleoprotein complexes. Although there are reported certain experimental results in favor of a greater or less degree of organ or protein specificity for these "nucleoproteins," yet these are offset by negative results obtained by other investigators. It is possible that the organ specificity observed, and best demonstrated by "saturation" or exhaustion experiments (Fiessinger, Beebe), are to be attributed to the organ specificity of cell proteins in general, which has been repeatedly demonstrated with simple organ extracts by similar saturation methods. The chemical considerations and my own experiences are opposed to accepting at this time the hypothesis that "nucleoproteins" possess a marked organ specific antigenic property, greater than that exhibited by cell proteins in general.

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* The complete article will appear in the Ztschr. f. Immunitätsforsch.

MULTIPLE PRIMARY MALIGNANT TUMORS, WITH A REPORT OF TWO CASES IN DOGS

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Multiple primary malignant tumors are comparatively rare. Götting, von Hansemann, Redlich and Reichman finding them present among malignant tumors in 0.2, in 0.4, in 0.4 and in 0.3 per cent. of the cases, respectively.

A great many of the so-called sarco-carcinomatodes are mixtures of two entirely distinct tumors, namely a sarcoma and a carcinoma, each having originated separately and later having so thoroughly mixed with one another as to give the appearance of a tumor of single origin. Such a case is Spencer's,[1] wherein a sarcoma and an adeno-carcinoma occur close together in the uterus, in places mixed, resembling a true sarco-carcinoma. A similar case is reported by Schöne.[2] Some of these cases then are indistinctly separated multiple primary malignant tumors.

It is the general conception at present that any one malignant tumor originates from one single primary focus, or in other words, that it is monocentric in origin. Peterson, however, from the study of serial sections of early malignant tumors, believes that a pluricentric origin is the rule rather than the exception. Wooley[3] reports a case of a carcinoma of both adrenals, in which there are in all, five primary foci of similar histological structure. The proximity of these foci, three being in one adrenal, supports Peterson's idea, and makes it plausible that foci still more closely set, would at a later stage in the growth of the tumor, be conglomerate and would obscure its multicentric origin. It is, of course, impossible to determine in tumors beyond their early

1. Spencer: Carcino-sarcoma Uteri, Trans. Obst. Soc., Lon., 1905 (47), 338.

2. Schöne, G.: Sarkom und Karzinom in einer Schilddrüse beim Hunde, Virch. Arch. f. path. Anat., 1909 (19), 169-176.

3. Wooley, P. G.: "Notes on Multiple Primary Tumors," Bost. Med. and Surg. Jour., 1903, cxlviii, 1-6.

growth, whether or not their original impetus was from a monocentric or a pluricentric origin. One cannot entirely exclude the possibility of local predisposition, which in a broader interpretation, indicates the susceptibility of a certain tissue; i. e., the skin, the fascia, or even a system of tissues, including for instance the mammae, ovaries, uterus and the tubes. Thiersch, Adami, Bucher, Warthin, Wooley and others, have mentioned local predisposition or susceptibility in explanation of the occurrence of distinctly separated though closely seated multiple primary malignant tumors.

The fact that multiple primary malignant tumors are often bilateral and symmetrical, is significant in many cases of a predisposition on the part of the tissue affected. This predisposition, Roger Williams believes, is a developmental disturbance. Zangmeister found that out of 39 sarcomas of the ovaries, 10 were primarily bilateral, while Pick found 9 bilateral instances out of a series of 23 sarcomas of the ovaries. In 15 cases of malignant testicular disease, Schubert found that 3 were primarily bilateral, while in a series of 114 similar cases, Kober found 5 instances of primary bilateral tumors. The fact that primary bilateral sarcomas of the ovaries and testicles are more apt to occur when the tumors develop early in the life of the individual, makes them of probably anomalous embryonal development. Rolleston and Marks, out of 26 cases of malignant disease of the adrenals, found that 2 cases were primarily bilateral. Walker found 10 primary malignant tumors out of a series of 141 malignant tumors of the kidneys. These and many other cases cited in the literature represent a class of cases which indicate that one certain type of tissue in the body may be predisposed to a malignant transformation under favorable circumstances. They indicate some anomaly in the embryonal development of that particular sort of tissue.

I have reviewed reports of 95 cases of multiple primary malignant tumors. Thirty of the 95 cases show no predilection for any particular system or type of tissue; 27 of these 30 cases are represented by both a carcinoma and a sarcoma, while 3 of the 30 cases are represented by but one type of malignant growth.

Thirty-four of the 95 cases occur in the reproductive system, including under this head, the mammae, ovaries, uterus, tubes and vagina; of these 34 cases, 16 are represented by both a sarcoma and a carcinoma, while 18 of the 34 cases show but one type of malignant tumor.

Thirteen other of the 95 cases reviewed, occur in the cutaneous system; 2 of these are each represented by a sarcoma and a carcinoma, while the remaining 11 are all represented by carcinomas alone.

Again, 13 of the 95 cases occur in the gastro-intestinal tract, including the esophagus, stomach, intestines, liver and the pancreas; of these 13 cases, 4 are represented by a sarcoma and a carcinoma, while the remaining 9 cases are represented by but one type of malignant tumor. In all 95 cases there are but 4 instances wherein more than 2 malignant tumors occur in the same individual.

Briefly, then, it is evident that two-thirds of all these cases of multiple primary malignant tumors are confined to systems, while but one-third of the cases are miscellaneously distributed. Certain benign tumors, that is, lipomas, ecchondromas, neurofibromas and fibromas, are often multiple; this indicates some susceptibility on the part of the tissue involved. Since no sharp line of separation can be drawn between the benign and malignant tumors, a comparison in the occurrence of multiple tumors in individuals of each class is of marked significance. Adami and Williams point out that in the female the involution of all the reproductive tissues at the climacteric brings these tissues to maturity much earlier than the tissues in the rest of the body, and hence exposes them to malignancy in a greater degree. The type of the tumor, as is seen from the above cases, is not so important a consideration of multiple primary malignant tumors, as is the system or tissue in which these tumors occur. Behind all the indirect causes of cancer, which when boiled down mean "irritation," there is something else which in the interpretation of to-day is called a "biological disturbance." This biological disturbance may lead to a local, to a tissue, to a system, or to a general predisposition to malignant growth. The first three conditions have been

illustrated above, while the fourth condition of general predisposition is brought out clearly in the work of Miss Sleye in collaboration with Dr. Wells at the University of Chicago. Their work, which has been the most extensive on the heredity of cancer in animals, goes to show that strains of mice born from cancer parents have a peculiar susceptibility to benign, and especially to malignant tumors; a sarcoma is as apt to crop out in these animals under conditions of chronic irritation as is a carcinoma. A chronic focus of infection in the lung of a normal mouse leads to a granulomatous nodule or perhaps a benign papilloma; in a cancer strain mouse the same irritation is much more apt to produce a malignant tumor. The strains of cancer mice have a greater incidence of malignancy among them than the non-cancer strain. Multiple primary malignant tumors are much more frequently found among the cancer than among the non-cancer strains. The best workers in the field of heredity in human cancer have so far failed to find any definite proof of a hereditary predisposition to malignancy.

Case reports: Very briefly, Dog A presents an adenocarcinoma of the thyroid gland with metastases in the lungs and in the region of the pineal gland; besides this there are bilateral adrenal hypernephroma (mesothelioma) associated with bilateral congenital cystic kidneys. The thyroid carcinoma is probably of indirect metabolic origin, as is indicated by (1) the frequent occurrence of carcinoma of the thyroid in goiter districts (Müller and Speese, Hinterstoisser, Limacher, etc.), and (2) by the work of Marine and Lenhart on brook trout, wherein carcinomas could be produced almost at will by disturbing the healthy conditions of the fish. The adrenal tumors in Dog A are typical adrenal mesotheliomas, each being entirely independent of the other, and also of the kidneys. Their bilaterality and also their association with bilateral congenital multicystic kidneys is strongly significant of a disturbance in the embryonal development.

Dog B presents a carcinoma of the thyroid gland and a mixed tumor of the mammary gland; the latter is quite like the mixed tumors so characteristic of the

parotid and submaxillary glands. In this tumor is found sarcomatous connective tissue at the edge, endothelial-like tubules lined with several irregular layers of cells, myxomatous tissue, and an imperfectly developed cartilage. Its composition, closely allied to the teratoma formations, makes it without much doubt of anomalous embryonal development.

In Dogs A and B then, the multiple primary malignant tumors belong to the class of miscellaneously distributed tumors, since no particular set of organs, tissue or system of tissues is involved, and since both the tumors in each animal are of different etiology.

November 10, 1913.

DIFFUSE, PHLEGMONOUS, "IDIOPATHIC" GASTRITIS

LUDWIG A. EMGE

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There are a number of excellent articles on this subject, and especially noteworthy for their completeness are those of Schnarrwyler,[1] Adams,[2] and Koenig.[3]

The disease is very rare; there are reported only about fifty cases of true "primary" or "idiopathic" phlegmonous gastritis. This is a surprisingly small number considering the long period during which they have been observed. A much greater number of reports dealing with phlegmonous gastritis in general have been published, but 50 per cent. of these concern secondary suppurative gastritis in which the origin of the infection elsewhere in the body and the portal of entrance into the stomach is obvious, as, for example, infected carcinomas, ulcers, etc. Such reports have not been considered in the review from which the following facts were collected: The streptococcus pyogenes was found in pure culture in 70 per cent. of all of these primary phlegmonous gastritis cases. In the remaining 30 per cent. the same organism was associated with the staphy-

1. Archiv. f. Verdauungskrankh., 1906, xii, 116.
2. Lancet, 1910, i, 293.
3. Deutsch. Med. Wchnschr., 1911, xxxvii, 631.

lococcus pyogenes albus and aureus, b. coli communis, or the pneumococcus.

In 75 per cent. of all cases a predisposing factor was mentioned; alcoholism in 25 per cent.; dietetic errors and food and drug-poisoning each 10 per cent; trauma, puerperal fever, chills (pyemia) and articular rheumatism, 4 per cent. each; erysipelas, bronchiectasis, alveolar abscesses apparently healed, typhus, undernutrition in the young, and ulcer of the leg, 2 per cent. each.

The male sex is more often attacked, the ratio being 5 to 1. As regards occupation, the class of day laborers was found to furnish 50 per cent. of all cases. This was accounted for by their habits of alcoholism and overeating. The greater number of cases, four-fifths, occurred between the ages of 20 and 40, the extreme limits being 11 and 76 years of age.

The symptoms are a sudden onset with general indications of a severe sickness. There is considerable pain in the gastric region, also a burning sensation not relieved by drinking. These are aggravated by profuse vomiting of a fluid which is often bile-stained and generally contains no blood. At the same time the temperature rises to 99 to 102 F., occasionally preceded by a chill and accompanied by an accelerated pulse.

Other symptoms have been described, among them a rigid abdomen, a high temperature of 105 to 106 F., local swelling tender to palpation, constipation, diarrhea with stools which do not contain any blood, and vomiting of the entire gastric mucous membrane. These last mentioned symptoms occur in only a few cases. The progress of the disease is rapid, the pulse increases in frequency, and feebleness and death, which in most cases is due to diffuse, suppurative peritonitis, generally follows coma.

From the symptoms it can be readily seen that a correct diagnosis is rarely made. The symptoms are common for many other pathologic conditions connected with the abdomen in general, and the progress of the disease is so rapid that it is not surprising that diffuse phlegmonous gastritis has been diagnosed in only about 5 per cent. of all cases, half of which were recognized

during exploratory operations. The remaining 95 per cent. were thought to be diffuse peritonitis, perforation of a gastric ulcer, localized abscesses, carcinoma of the stomach, perforating appendicitis, appendiceal abscess, or acute pancreatitis.

As to treatment, Johnson, in his "Surgical Diagnosis,"[4] suggests early operative drainage.

Koenig[5] saved a patient by extirpation of the entire stomach. Spontaneous recovery is reported in one case.

The average duration of this disease is from three to seven days. The extreme limits are twelve hours and two weeks. The mortality is 95 per cent.

Idiopathic phlegmonous gastritis, as the name indicates, is limited to the stomach, the walls of which are greatly thickened, heavy and boggy. The mucosa is generally pale and swollen and its folds may be absent or indistinct. Perforations are generally absent except in cases of several days' duration, in which perforations from the submucosa out do occur. The entire mucosa may be raised from its bed by undermining suppuration. The submucosa has been greatly increased in thickness being often as much as half an inch thick. It is almost white or yellowish-green in color, usually firm and solid, and a peculiar, pea-green pus can be expressed from it. The muscularis is pale and occasionally swollen. No gross changes will be seen on the serosa unless a perforation has occurred.

Naturally, peritonitis is the commonest associated lesion. The infection is supposed to spread to the peritoneum by way of the lymphatics soon after the manifestation of gastric symptoms. The rapid progress of the infection is best explained by the great virulence of the infecting bacterium.

Histologically, there are masses of leukocytes present between the glandular structures. The latter in general appear normal. The blood-vessels are dilated and occasionally the entire mucosa may be necrotic, especially in cases of several days' duration. Great numbers of polymorphonuclear and mononuclear leukocytes infiltrate

4. A. B. Johnson: Surgical Diagnosis, New York, 1910, first Edition, p. 55.

5. Deutsch. med. Wchnschr., 1911, xxxvii, 631.

Fig. 1.—A vertical section through the entire thickness of the stomach. The submucosa is markedly increased in width and the tissue-spaces are abnormally large. The large strands of muscle fibers of the muscularis are more widely separated than normal. Note the sharp lines of demarcation of the submucosa against the mucosa and muscularis (dia. 5).

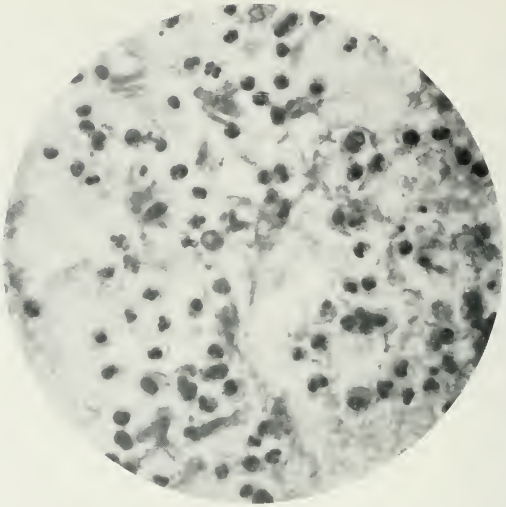

Fig. 2.—(500 ×). The structure of the submucosa is lost. The original elements are replaced by an exudate rich in mononuclear and polymorphonuclear leukocytes (dia. 500).

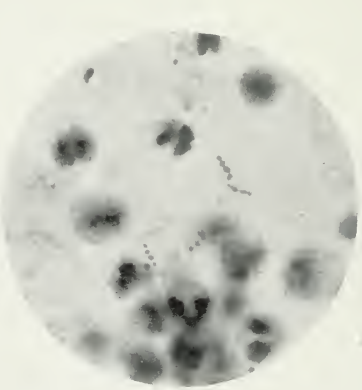

Fig. 3. Chains of Gram-positive cocci found in the sections in the submucosa (dia. 1200).

the submucosa to such an extent that with the abundance of fibrin present the original structure of this layer is completely obscured. The muscularis mucosae is often swollen; bacteria have been repeatedly found. Little or no change occurs in the muscularis. The muscle-bundles may present signs of a beginning pressure necrosis, and the individual bundles occasionally are pushed apart by masses of round cells. The serosa is rarely altered. Patches of fibrin on the serosa may be found if perforation has taken place.

An example of this disease was encountered last March in the Cook County Hospital here. A. B., a tailor, 67 years old entered the service of Dr. Kunz in Ward 20, on March 11, in order to have a fracture of the left clavicle attended to. Except for this trouble the examination was negative. The family history and personal history contained nothing noteworthy, and the personal habits were those of an ordinary workman.

He felt well up to March 23, when he suddenly began to complain of pain in the gastric region. An hour or so later he started to vomit profusely and examination revealed rigidity, tenderness, and tympany over the epigastrium and hypochondrium. There was also a sense of fulness in this region, but no tumor could be felt. The heart-sounds were feeble, the temperature rose to 106 F., and breathing became labored and fast; acute hemorrhage and pancreatitis were thought of. He gradually became comatose and died at about 3 o'clock the next morning, March 24.

Post-mortem examination was made five hours after death and the following conditions found: "The lining of the stomach is smooth. The wall is very thick averaging one centimeter. There are no folds in the lining and no perforations. The wall is soft and from the surfaces made on sectioning the stomach wall across, a greenish-yellow pus is expressible. The swelling stops sharply at the pyloric ring. Such surfaces are light pea-green." . . . After careful examination, no changes were found in the trachea, proximal portion of the esophagus, larynx, pharynx and tonsils. Except a generalized fibrino-purulent peritonitis no other alterations which could be connected with the changes in the

stomach walls were found. The fractured clavicle was in process of normal healing.

Microscopic examination confirmed the anatomical diagnosis, i. e., acute phlegmonous gastritis.

Figure 1 is a photograph of a cross-section of the stomach-wall. The great thickness of the submucosa is evident, having increased over five times. The mucosa, muscularis and serosa on the other hand are apparently normal in thickness.

Under higher magnification the glandular structures are normal. There are few polymorphonuclear leukocytes seen in the masses of mononuclear leukocytes normally present in this layer. The submucosa consists simply of fibrin and leukocytes among which the polymorphonuclear variety prevails. The original structures of this layer save the muscularis mucosa cannot be distinguished (Fig. 2). This condition stops abruptly at the muscle-layer, the fibers of which appear normal, although there are many round cells present between the bundles which are more widely separated than normal. There are no changes in the serosa.

Long and short chains of Gram-positive cocci were found throughout the submucosa only (Fig. 3). The streptococcus pyogenes was isolated in pure culture from pus which flowed into incisions made when the stomach-wall was cut across.

In conclusion, it seems appropriate to emphasize the great similarity to erysipelas and to phlegmonous inflammations of the subcutaneous tissues other than erysipelas, also the small size of the stomach and the failure to find any primary distant infection for which this instance of phlegmonous gastritis was secondary.

November 10, 1913.

OCCLUSION OF THE AORTIC ARCH AT THE ISTHMUS — COARCTATION AORTAE

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(From the Pathological Laboratory of the Rush Medical College.)

On March 14, 1913, a cook, 42 years old, entered the service of Dr. Amerson in Cook County Hospital with symptoms of marked disturbance of the circulation, slow and

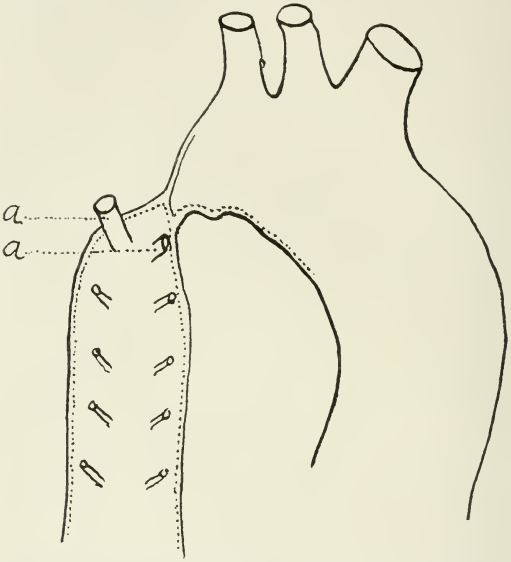
stertorous breathing, systolic murmurs at the apex and over the aortic area, slight icterus and cyanosis.

He was in a stupor and unable to give any clear account of his illness; friends said he had been treated for syphilis. He lived only thirty-five hours and during most of this time the pulse ranged from 100 to 136. During the last twelve hours of life a fever developed with gradual rise of temperature to 103.8 F. per rectum. The clinical diagnosis was "organic heart disease with complications, acute fibrinous pericarditis, pulmonary hypostasis, gangrene of the leg."

Anatomical Diagnosis: Occlusion of the aortic arch at the isthmus; marked compensatory dilatation of the *arteriae mammariae internae* and *aa. intercostales III;* obliterative fibrous pericarditis; passageway between the loosened anterior and right posterior aortic cusps between the loosened anterior left ventricle; large, deep ulcer of the left leg; marked catarrhal bronchitis and bronchopneumonia of the dependent portions of the lungs; slight fibrinous pleuritis; marked emphysema of the lungs; goose-fat clots in the pulmonary artery, the right ventricle and auricle; cloudy swelling and fatty changes of the liver and kidneys; hyperplasia of the spleen; edema of the brain and small bowel; minimal degree of sclerosis of the root of the aorta; remnant of the left fetal valve at the upper margin of the mouth of the superior vena cava; small network at the site of the Eustachian valve; small network over the fovea ovalis in the right auricle; regions of fibrous thickening in the anterior mitral leaflet; small papilloma on the anterior chest wall; unequal dilation of the pupils; missing teeth and gold crown on three teeth; fibrous adhesions between the gall-bladder and the hepatic flexure of the colon, between the under surface of the right lobe of the liver and the colon.

When the trunk was opened by the usual median incision in front and the skin and subcutaneous tissue dissected away from the thorax and everted to expose the abdominal organs, the *musculi recti abdominales* were cut across as is customary just below the costal arch. When this was done the large size of the *arteriae epigastricae superiores* was noticed immediately; their large channels where they were severed furnished a warning that caution should be used and the real cause of some unusual condition in the organs of circulation ascertained before irremediable damage had been done by cutting in the wrong place or the wrong way. These arteries 4 cm. below the costal arch had a circumference of 1.4 cm., fully three or four times larger than normal.

The heart weighed 560 gm., the increased weight being chiefly due to increased thickness of the left ventricle wall and caused in part, at least, by the increased pressure in the aortic arch because it was completely occluded at the isthmus (See Fig. 1). This increased pressure was also responsible for a passage-way under the common attachment to the aortic



Illustrating the form of occlusion at the isthmus reported. The dotted lines represent the inner wall of the aorta. *a*, The very large uppermost intercostals from the aorta. Arteriae intercostales III. as seen from behind.

wall of the anterior and right posterior cusps. When these two cusps did their part in supporting a column of blood during diastole and in closing the aortic outlet, their free margins failed to meet any nearer to the aortic wall than 1 cm., for their mutual attachment here was gradually lengthened by this increased pressure and beneath this band the pockets or sinuses of Valsalva for these two cusps communicated by an opening 10 by 15 cm.

Lesions of the aortic valves are common with stenosis at the isthmus or coarctation aortae as it is sometimes called. By most writers they are referred to as chronic aortic endocarditis, and mention is rarely made to any possible relationship between these valvular changes and increased tension in the arch. These changes in the valves in many instances of coarctation are probably the results of repair, of thrombosis and organization in minute ruptures of the leaflets. In contrast to inflammatory conditions such as the infectious endocarditides, the alterations in the aortic valves with coarctation are generally within the sinuses and not on the ventricular surfaces. The interpretation I have made of the passage-way between the two adjacent sinuses Valsalvae is with a full realization of the frequency with which congenital malformations here are also associated with coarctation.

"At the occlusion the aorta has an appearance as though a rather heavy twine had been tied about it for some time distal to the mouth of the left subclavian artery and then removed. The constriction is hour-glass shaped and continues along the aorta for a distance of 5 cm. The external diameter, where the lessening in size is most marked at the bottom of the annulate groove, is 8 mm. If paraffin were poured into the aorta on each side of the occlusion and moulds made, they would be rather abruptly pointed and while still in the aorta would overlap, the tip of the lower or distal extending a little above the other and on the left side of it. There is a small pouching of the proximal funnel of the aorta where the *ductus arteriosus* cord joins it externally; the ductus is completely closed. In the lining here where this cord joins the aorta there is slight calcification."

Various observers have discussed the frequency with which arteriosclerosis occurs here where the ductus formerly opened; it is often referred to as a place of lessened resistance.

"The two uppermost intercostal arteries are very large and have thin walls as though in the collateral anastomosis they had functionated as veins and the blood had been poured into the aorta here at the proximal end or top of the channel distal to the occlusion. The mouths of the intercostal arteries directly below are slightly larger than usual. The internal mammary arteries are fully four times larger than normal."

For comprehensive accounts of this anomaly and for the literature the reader should consult Maude E. Abbott's article in Osler's Modern Medicine and those of Monckeberg,[1] Sella,[2] and Strauer.[3] There are about two hundred instances of stenosis of the isthmus reported, and about two-thirds of these have been found in the bodies of persons living one or more years. Abbott mentions only twenty found in adults, or of this class, the so-called "adult type," in which the channel in the aorta was completely obliterated.

Although not incompatible with life it imposes an increased hazard on the individual, for spontaneous rupture of the aorta is frequently a sequence of stenosis or occlusion at the isthmus. The large size of the *arteriae epigastricae superiores* just below the costal arch and their pulsation is of great clinical moment.

November 10, 1913.

REPLACEMENT OF THE HIS BUNDLE BY ADIPOSE TISSUE *

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(From the Pathological Laboratory of Rush Medical College.)

Numerous studies have established a definite relationship between the symptoms usually referred to as Adams-Stokes syndrome and changes in the auriculo-ventricular bundle of the heart. These changes may be classified as progressive and regressive. The first type are usually inflammatory and often follow acute infections. Under the head of regressive or senile changes are fibrosis, atrophy and adiposity. These lesions are perhaps a result of the age of the patient. They arise and develop in the bundle fibers more frequently than in the myocardium so that the bundle may be considered a seat of predilection. This may be due to its blood-supply, which is independent of other portions of the myocardium.

1. Verhandl. d. d. path. Gesellsch., 1908, xii, 242.
2. Ziegler's Beiträge, 1910, lxix, 501.
3. Deutsch. Arch. f. klin. Med., 1909, xcv, 344.

* The complete report appears in the Archives of Internal Medicine, 1914.

Changes in the bundle may develop and fail to give rise to the Adams-Stokes syndrome. Only a portion of the symptoms regarded as essential for the diagnosis may be manifested. Thus only a lengthening of the intersystolic period or bradycardia, tachycardia, arrythmia or cyanosis may be present.

Fatty changes have been found in the specific conducting system in people who have died suddenly. Mönckeberg, Ashoff, Tawara, Fahr, Sapegno and others have reported numerous cases, nearly all of which followed acute infectious diseases such as pneumonia, typhoid fever, bronchitis, septicemia, diphtheria, rheumatism, influenza, etc. All of these reports concern acute fatty metamorphosis and have nothing to do with another retrogressive change, lipomatosis or adiposity.

There can be found in the literature at least three cases of adiposity of sufficient degree to give rise to cardiac symptoms. Fahr has recorded an instance of Adams-Stokes syndrome in which, after death, a marked lipomatosis of the bundle region was found. Ashoff and Tawara report a similar observation. Sapegno has described a case of marked adiposity, the patient dying suddenly, death being ascribed to the changes in the bundle region.

I examined the auriculo-ventricular system of a man 38 years of age who died suddenly. He was an exceptionally powerful and well-developed white male, who had always been well, and so far as known had never sought medical advice. After death it was learned that he occasionally had brief attacks of trembling during which the hands were moved jerkily and violently. There was no falling or loss of consciousness during these attacks and they lasted but a few moments.

On post-mortem examination there were no gross evidences of marked disease anywhere. There were no evidences of poisoning, nor did the circumstances attending death indicate this. On gross examination the heart was normal, except for slight nodular sclerosis of the coronary arteries and slight fibrous myocarditis.

Dr. E. R. LeCount, who conducted the post-mortem examination, was of the opinion that the gross changes were altogether inadequate to explain death and for this

reason study of the His bundle was undertaken. Histological examination was carried out by means of serial paraffin sections of the entire His bundle down to and for a considerable distance beyond the point of origin of the right and left branches. Further study was made of the terminal extensions at various levels in the ventricular walls. Every fifth section was mounted and various stains employed.

In such sections there is a very marked fatty infiltration limited strictly to the auriculo-ventricular bundle and its branches, the myocardium containing no adipose tissue. This change is moderate in the nodal region, more marked in the main stem. At the point of division of the main stem into right and left rami nearly the entire bundle is absent and in its place there is adipose tissue. Both of these branches and the Purkinje fibers at whatever plane examined present such alterations in varying degree.

Both the muscle fibers and the connective tissue of the bundle system are replaced by adipose tissue. If that part of this "specific conducting system" lying between the proximal part of the node and the point of origin of the right and left branches is arbitrarily divided into three segments, then approximately 20 per cent. of the fibers and connective tissue framework of the first segment of the bundle is replaced by adipose tissue, 65 to 70 per cent. of the middle segment and 85 to 90 per cent. of the distal segment is similarly affected. Just distal to the bifurcation of the bundle the replacement of the left branch with fat is not marked, but 10 to 15 per cent. of its structure being so replaced, whereas at a similar location in the right branch 50 per cent. of the fibers are so affected. These alterations are present, as before stated, in the terminal portions of this specific system of muscle fibers throughout their subendocardial course. The adipose tissue, limited sharply to the Purkinje fibers, differentiates this system at a glance from the surrounding myocardium; in fact, their location is readily determined with a hand lens or the low power of the microscope and followed from section to section by the adipose tissues, by the fat holes at such points.

Some of the muscle cells of the Purkinje fibers are normal. Others, on cross section, show fat globules in their centers. These globules vary in size from small droplets to larger drops, which replace a portion of the protoplasm, leaving the fibrillae standing out very sharply about the periphery of the cell. Again, the fibrillae may divide the cell into small fields, the center of these fields being completely occupied by fat droplets. Or the muscle cell may be so distended with fat globules that the remaining fibrillae have all been crowded into one corner of the cell, many of them absent. Finally, the entire muscle fiber with its fibrillae, cell membrane and surrounding sheath of connective tissue may be entirely absent and its place taken by adipose tissue.

In conclusion, without attempting to predicate that death in this instance was due to these alterations in the His bundle, it is believed that such an examination as this in instances of sudden death with symptoms of cardiac disease and where there are relatively few gross changes in the heart, should be more frequently made.

November 10, 1913.

BRAIN ABSCESS CAUSED BY FUSIFORM BACILLI *

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AND
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A report by one of us[1] concerning a number of processes, with which fusiform bacilli were found associated, included three cases of meningitis and one cerebellar abscess. On account of the fact that these organisms were accompanied by streptococci and were, when isolated, non-pathogenic for animals, it was impossible to decide whether or not the fusiform bacilli caused the lesions or were saprophytic invaders of a process caused

1. Dick, George F.: Fusiform Bacilli Associated with Various Pathological Processes, Jour. Infec. Dis., 1913, xii, 191.

by the streptococci. An opportunity for additional information was afforded by the following:

History.—A man aged 40 was admitted to the service of Dr. Dean D. Lewis at the Presbyterian Hospital suffering from severe headache on the left side associated with difficulty in speech. He had had a drainage of a temporosphenoidal abscess three months before that time, with recovery. This had been preceded by a chronic bronchitis. The second abscess was opened and a quantity of foul-smelling pus obtained from which cultures were made. The patient died about a week after the drainage of the abscess. The necropsy report was as follows:

Anatomic Diagnosis.—Cerebral abscess, chronic and subacute leptomeningitis, recent and healed operative wounds in the scalp and calvarium, petechial hemorrhages of the heart, stomach and intestine, edema and hypostasis of the lungs, cloudy swelling of the heart and liver, fibrous adhesions between the stomach and pancreas, and between appendix and peritoneum, subacute and chronic follicular enterocolitis, Meckel's diverticulum.

At the base of the nose is a circular opening in the skull 3 cm. wide, the margins of which are smooth. The dura and pericranial tissues are adherent, and the former is markedly thickened at this point. Just above the left ear is a linear incision, coronal in direction, 7 cm. long, the lower 4 cm. of which are gaping. The wound leads into an abscess-cavity located in the left cerebral hemisphere just anterior to the fissure of Sylvius. When the brain is removed, about 125 c.c. of a foul-smelling, dirty gray pus escapes. The ears and accessory sinuses are free from purulent material.

The brain is of normal size, weighing about 1,600 gm. The left hemisphere is somewhat larger than the right one. An abscess varying in width from 0.5 to 2 cm. follows the course of the left Sylvian fissure and extends into the temporal, frontal and parietal lobes of the same side. It is filled with a brownish-green mass and ends within the left occipital lobe. The left lateral ventricle is compressed and half as large as the right, which is of the same size. The lesion separates the temporal lobe almost completely from the rest of the cerebrum and breaks into the left lateral ventricle at the beginning of the occipital lobe. The tissues of the affected lobes are infiltrated with brownish and greenish patches which replace the white and gray matter to a considerable extent. The cerebellum was found to be of normal size and without gross lesions.

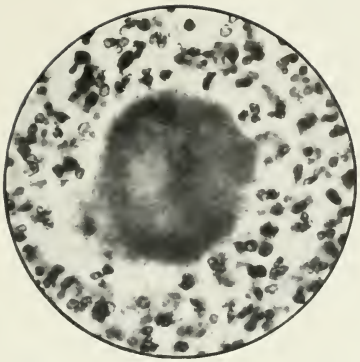

Fig. 1.—Actinomyces-like mass of fusiform bacilli in brain abscess; × 650.

Fig. 2.—Fusiform bacilli from pure culture on blood-agar; × 1,200.

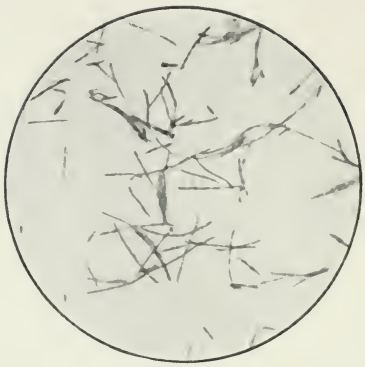

Fig. 3. Fusiform bacilli from pure culture on blood-agar; 1,200.

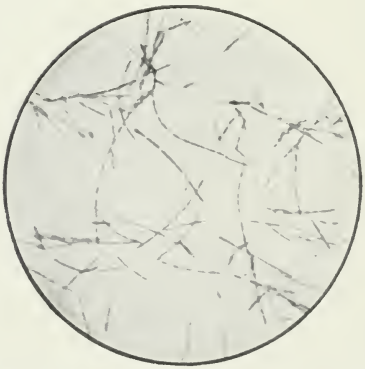

Fig. 4. Fusiform bacilli from pure culture on blood-agar; 1,200.

Examination.—A number of pieces from the sides of the lesion, hardened in formaldehyd solution, were examined microscopically. The most marked changes are found in the middle and posterior third of the medulla and cortex of the left temporal lobe about the fissure of Sylvius. Especially conspicuous are the many large and small areas of necrosis which involve both the white and gray matter. These areas of necrosis are generally sharply demarcated and limited by a zone of fibrous connective tissue. There is also a marked accumulation of polymorphonuclear leukocytes which extends well into the gray matter, which for the greater part is broken down. Larger and smaller fields of recent hemorrhages are present throughout this region.

Between the necrotic areas as well as in the accumulation of polymorphonuclear leukocytes circular masses are seen which simulate in a measure an actinomycotic formation when observed under low magnification. They are invariably surrounded by heavy walls of small round cells and polymorphonuclear leukocytes. Under high magnification these masses are seen to consist of a great number of long slender filaments which radiate about a small ball of central members. Stained with hematoxylin and eosin, an outer small zone which takes the pink stain seems to consist of fine fibrin threads which spread between the surrounding cells. With connective-tissue and fibrin stains (Mallory-Weigert and Weigert-Mallory) it can be made out that these threads are not fibrin but the outer ends of the filamentous organisms The organisms are Gram-negative when stained by Mallory-Wright and by Weigert's modification of Gram's stain. The groups of organisms vary in number as indicated by the size of the groups, the larger of which are found within the necrosed areas while the smaller groups are limited to the free accumulations of pus.

Anaerobic cultures made from the pus as obtained at the operation yielded a pure culture of fusiform bacilli. The organisms developed in from two to four days on the surface of ascites or blood-agar slants as small drop-like colonies which grew to be about a millimeter in diameter raised well above the surface of the medium. The growth in the water of condensation formed rather discrete colonies in the fluid. In ascites-agar stabs there was no outgrowth into the surrounding medium. The organism did not grow on ordinary media without serum or blood. The organisms were Gram-negative, at times distinctly fusiform and rather short, with vacuoles and granules; at times large filaments were formed.

A pure culture from one of the original colonies on blood-agar was injected into the brain of a rabbit. In about twelve hours the animal developed chronic convulsions and died in about thirty-six hours with paralysis of all four extremities. The meningeal fluid was found at necropsy to be rich in polymorphonuclear leukocytes, and fusiform bacilli were found in smears and cultures from the fluid. The lateral ventricles were filled with thin pus, from which the organisms were also recovered in pure culture. A slant of this culture was injected into the brain of a second rabbit, and this animal died in much the same way as the first. In this animal a small abscess was found just outside of the right lateral ventricle, with necrosis of the surrounding tissue. The tissue was examined for actinomyces-like bodies similar to those described in the necropsy, but none were found. Two rabbits injected intrameningeally died in about thirty-six hours in convulsions. In these rabbits there was very little exudate on the meninges, but only a diffuse hyperemia. At this point a contamination of the strain which was being passed through rabbits occurred, and experiments were resorted to with subcultures from the original growth, which had been growing over a month. Injection of a culture of these organisms into the meninges was without result. Later it was found that intrameningeal injections of the growth from a dozen slants were apparently harmless for rabbits. One animal received three injections of large quantities of the organisms with no harmful results. The cultures had lost their pathogenicity. It is not improbable that the readiness with which pathogenicity is lost in these organisms explains the negative results of attempts to produce lesions in animals, as the isolation in pure culture of fusiform bacilli is often time-consuming.

The finding of the actinomyces-like bodies in an abscess from which pure cultures of fusiform bacilli were obtained has direct bearing on the identity of the so-called ray fungi commonly found in tonsils. These bodies have been commonly mistaken for actinomycelial granules. Davis[2] believes these granules to be composed of streptococci, spirilla and organisms of the fusiform group.

The filaments composing the bodies found in the brain in this case resemble closely the organisms cultivated from the pus containing them.

Jan. 12, 1914.

2. Davis, D. J.: Personal communication.

BACILLUS WELCHII IN BLOOD CULTURES WITH RECOVERIES

ALBERT HOWARD BAUGHER

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The purpose of this paper is to report four cases in which the bacillus aërogenes capsulatus was obtained in blood-culture during life and to call attention to this means as a valuable method of diagnosis. Since the discovery of this organism there seems to have been no doubt but that it invaded the general blood-stream at or shortly before death, as is evidenced by its generalized presence at autopsy in patients dying from this infection. Welch and Nuttall[1] made this observation and called attention to it in their early report. But notwithstanding this report and the suggestion that it carried, only a few of the many observers of this organism have reported positive blood cultures due to it. And so far as I have been able to find there has been no recovery reported when a positive culture was obtained.

In my series of four cases, three recovered and one died. But in no instance did operation or death occur prior to the reporting of the positive blood-culture.

In 1896 Flexner,[2] in his study on terminal infections, said that there was evidence of the distribution of the bacilli within the body during life, but that he was reluctant to admit of a general invasion of the blood and tissue before death, as the maintenance of life for any length of time after the organism had established itself in the blood and produced gas there, was probably impossible. But Gwyn,[3] in 1899, by repeatedly recovering the organisms from a patient during a space of thirteen days, thought that it was impossible for gas to be formed in the circulating blood. And Cole,[4] in 1902, connected the vein of a moribund patient suffering from a generalized infection with a rubber tube and allowed 20 c.c. of blood to flow out under water and thus demon-

1. Welch and Nuttall: Bull. Johns Hopkins Hosp., 1892, iii, 81.
2. Flexner, Simon: Jour. of Exp. Med., 1896, i, 559.
3. Gwyn, N. B.: Bull. Johns Hopkins Hosp., 1899, x, 134.
4. Cole: Bull. Johns Hopkins Hosp., 1902, xiii, 234.

strated that no gas escaped. This data seemed quite conclusive that gas was not formed in large quantities at least during life, and has not yet been disproven so far as I am aware.

A brief review of the instances recorded in which positive blood cultures have been obtained follows.

Gwyn,[5] in 1899, recovered this organism on three different occasions from the blood of a patient with a clinical diagnosis of "chorea insaniens." The first culture was obtained thirteen days before death, and in the third the streptococcus was associated. Acute endocarditis was now added to the diagnosis.

Cole,[6] in 1902, obtained the organism from the blood three hours before the death of a man who had had both legs crushed two days previously. He used 8 c.c. of blood, 1 c.c. of which was injected into the ear vein of a rabbit, the remainder divided equally between twelve tubes of litmus milk. Both the rabbit and the culture media gave a positive result.

Schiedler,[7] in 1909, attempted a culture in a post-partum case, but with negative results, both aërobically and anaerobically.

Rhea and Young,[8] in 1909, reported two cases of infection due to bacillus aërogenes capsulatus following abortions, one of which gave a positive blood culture eighteen hours before death.

Libman[9] attempted to cultivate this organism from the blood of a patient with gall-bladder infection, both by cultures and by inoculating a rabbit, but with negative results.

Hewitt,[10] in 1911, reported ten cases of gas bacillus infection in which he obtained four positive blood-cultures. But he does not state the time at which these cultures were taken in regard to the time of death of the patient, all four of which died, one twelve hours

5. Same as 3.
6. Same as 4.
7. Schiedler, F.: Monatschr. f. Geburtsh. u. Gynäk., Berlin, 1909, xxx, 714-724.
8. Young, E. B., and Rhea, Z. J.: Boston Med. and Surg. Jour., 1909, clx, 401-404.
9. Libman, E.: Bull. Johns Hopkins Hosp., 1906, xxvii, 215.
10. Hewitt, W. R.: Jour. Amer. Med. Assn., 1911, lvi, 959-962.

after admission, the second fifty-eight, the third seventy-two and the fourth ninety-six hours. Since it is generally conceded that the incubation period of this organism is forty-eight hours, none of his culture could have been taken more than two days before death and it is more probable that they were taken on the day of death.

The essential facts of the cases are as follows:

Case 1.—Male, aged 51, contractor, was seen in consultation by Dr. L. L. McArthur, in whose service he entered the hospital May 16, 1912. He took sick rather suddenly three weeks previously with severe cramp-like pains in the region of the gall-bladder. The pain radiated to the right shoulder and downward. This attack lasted two hours. There was no nausea or vomiting at this time, nor in the subsequent history. The patient does not know whether he had temperature or not, but says that he was distinctly tender over the gall-bladder and in the epigastrium. This tenderness never disappeared entirely, but there were no more severe or sudden attacks or pain. He gave no history of constipation, jaundice, venereal disease or other ill health.

The examination on entering the hospital showed the following: temperature, 103.4 F.; pulse, 96; respirations, 28. Tenderness over a palpable mass in the region of the gall-bladder and epigastrium with some rigidity. Abdomen slightly distended. Leukocyte count, 8,050.

The patient was kept under observation for a week. At times during this period he was irrational and delirious and his temperature oscillated between 99 and 102.4 F. He did not experience much pain, but was restless. His mental condition in regard to his own feelings was that of a state of "well-being." A slight jaundice developed during this week of observation, and for this reason the blood-culture was suggested. The stools were normal, except that blood was found on one examination. The leukocyte count rose to 12,500, with 85 per cent. polymorphonuclears. The blood-culture was made five days before the operation and yielded the *Bacillus aërogenes capsulatus* and the *B. mucosus capsulatus*. The operation revealed a ruptured gall-bladder with about two-thirds of the fundus gangrenous, a large abscess beneath the liver containing thick, yellowish, bile-stained pus and two pea-sized gall-stones. The pus had a very foul odor and smears revealed the same organisms as found in the blood, and in addition a small Gram-negative bacillus, a fusiform bacillus and cocci. The patient recovered.

Case 2.—Male, aged 40, American, was seen in consultation with Dr. Edwin Tuteur on Feb. 2, 1913, at Henrotin Hospital, at which time a positive blood-culture was obtained. The

patient had been sick for five weeks with high fever, and six days previously had been operated on for cholecystitis and drainage established. The drainage tube was removed on the second day following the operation and the wound was allowed to close, although the patient's condition was growing more serious all the time. The report of the positive culture was given at the end of twenty hours. February 4, I was given permission to probe the wound, at which time a serous discharge, pus cells, bile and the *B. aërogenes capsulatus*, along with a few other organisms, were found. The patient continued to grow worse, although drainage was reestablished in the wound. February 18 to 21 the patient experienced severe griping pains in the bowels and passed large yellow bowel movements, with some blood and mucus.

February 18, Dr. A. E. Halstead saw the patient in consultation with Dr. Tuteur and Dr. McQuinn, and advised a second laparotomy. February 21 the patient was transferred to St. Luke's Hospital, where he was operated on by Dr. Halstead, February 22. Many adhesions were found in the region of the gall-bladder, and the anterior wall of the stomach and pylorus was greatly thickened. The scar and fistula were removed and drainage established. The discharge was very free following the operation, and February 28 was slightly acid, but did not give the silver nitrate test for hydrochloric acid. A later test, February 26, however, showed the discharge to be 10 degrees acid. February 27 it was 18 degrees acid, and a white precipitate formed on adding silver nitrate. The diagnosis of a gastric fistula was now made and the *B. aërogenes capsulatus* was still present in smears made from the discharge. The patient presented a hazardous condition for some time, but recovered. The fistula, though nearly closed, was present on discharging the patient March 26, 1913.

Case 3.—Male, aged 30, was admitted to the service of Dr. Frankenstein on May 15, 1913, complaining of sharp, cutting and continuous pain in the right chest. The pain was such that he could not lie down with comfort. The present trouble started four weeks ago, on which date in another hospital he had a fistula leading to the gall-bladder region curetted. On this same day he started for Chicago, but became violently sick on the train and had to stop in a small town for one week before he was able to leave, and on reaching here was treated for two weeks for pneumonia before entering the hospital.

A fluoroscopic examination by Dr. Case at St. Luke's Hospital on May 16, in the standing position, showed the right chest to be filled with fluid to within 1½ inches of the apex

of the cavity. Aspiration, however, on the same day did not permit any fluid to escape, but on the end of the trocar was a drop of bloody pus, which in smears revealed a small Gram-negative, a fusiform bacillus and the *B. aërogenes capsulatus*. On May 17 a positive blood-culture was obtained, which was reported on the following day. Exactly two days after the blood was taken for the culture, a rib was resected which allowed a large amount of pus to escape. The leukocyte count previous to operation ranged around 16,000, with 90 per cent. polymorphonuclears. The patient recovered.

The patient, in giving his history, stated that he had had three operations previous to the curetting mentioned above, the first being two and one-half years ago to drain an appendiceal abscess, another to remove the appendix and the third to remove the remaining stump of the appendix.

Case 4.—Male, Italian, aged 20, was shot through the lower end of the thigh with a rifle causing a compound fracture of the femur on the night of May 26. The wound was dressed by a physician, who put a through-and-through drain in the channel made by the bullet. Forty-eight hours after the accident the patient was admitted to the service of Dr. L. L. McArthur at St. Luke's Hospital. Immediate amputation was advised, notwithstanding the great sepsis of the patient. This was refused. The condition of the patient, aside from being very septic when admitted, was also very dirty and unkempt. Fecal matter was found on the dressings and on his clothing. The wound was exuding a bloody serum and crepitation could be elicited around it. The leg was beginning to become gangrenous. The dressing and drainage material had not been changed since being applied. Ten hours after admission blood was taken for a culture, of which 5 c.c. gave a luxuriant growth of the *B. aërogenes capsulatus* by the following morning.

In this case the blood was taken twenty-six hours before the patient died and was reported on twelve hours prior to death. On this day the leg was definitely gangrenous, gas could be expelled from the wound in large quantities, and distinct crepitation could be felt over the entire leg, thigh and abdomen to navel. The patient was not jaundiced before death, but immediately afterward a slight hemolytic tint was observed on the skin. The sclera were clear. Death occurred three and one-half days after the injury.

Each blood-culture was made from about 10 c.c. of blood, which was divided about equally between two flasks, each containing approximately 50 c.c. of broth. Both plain and glucose broth was used. In two cases I failed to receive a growth except in the flasks containing glucose. And in Case 4, in

order to make more certain as to whether or not the blood contained the organisms at the time of examination, 5 c.c. of blood was defibrinated and 3 c.c. of the defibrinated serum and corpuscles injected into the ear vein of a rabbit. The rabbit showed the characteristic findings due to this organism at the same time that the blood-culture was reported.

The cultures were pure, except in the instance in which the *B. mucosus capsulatus* was associated. No attempt was made to secure anaerobic conditions other than that which the depth of the media afforded. Smears from the bottom of the flasks showed the organisms in small numbers and usually in pairs. A chain was rarely found, as is characteristic in pus. Hemolysis was present in all the flasks that contained the organisms and in the flasks containing glucose, bubbles of gas were adherent to the sides of the flask, and occasionally they could be seen to rise to the surface of the broth. Capsules were demonstrated with difficulty in the organisms from the flask.

To prove the identity of the bacillus, rabbits were injected into the ear vein with 3 c.c. of the blood-culture medium from each of the four cultures. They exhibited the typical findings due to the *B. aërogenes capsulatus* after being incubated for eighteen hours. Smears from the various organs and heart's blood demonstrated that the bacillus was encapsulated, as did also the smears from the original pus.

The purpose of this paper is not to prove whether or not this organism is capable of multiplying in the circulating blood, or to call attention to its wide distribution in wounds and other pathological conditions, but to show that it is possible to demonstrate this organism by means of blood-cultures in severe cases of infection due to it, and yet obtain recovery when proper surgical treatment is instituted.

Feb. 9, 1914.

AN IMPROVED METHOD OF MOUNTING MUSEUM SPECIMENS

L. ENOS DAY

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From the time that pathology was first established as a science, teachers and workers in this branch of medical science have endeavored to preserve the tissue so

that the pathological changes could be demonstrated in the gross specimen. In order that the specimen may be of greatest value, the color, as well as the structure, should be preserved, as much depends on the color in demonstrating macroscopical pathological changes. The method which preserves the color best without destroying the structure of the tissue is the one desired.

Alcohol of various strengths is probably the oldest substance used in preserving museum specimens. Its use, however, has the great disadvantage of not only shrinking the tissue, but rapidly destroys the color. Some years ago we welcomed with delight the statement that formalin would meet our desires as a preservative for museum specimens. The results, as we all well know, did not meet with our wishes. While it is true that it prevents decomposition even in quite dilute solutions, it does not preserve the color and causes some shrinking and renders the tissues quite brittle, when used alone. It has, however, the advantage of being much cheaper than alcohol.

It was not until Professor Kaiserling published his method of preserving museum specimens that we were able to preserve the original color in pathological or normal tissue for any length of time. At the present time I know of no method which preserves the color and structure better than this one. Since this method was first published, a number of modifications have been recommended, but none of them have proven to be any special improvement over the original formula. This method has the disadvantage of being bulky, the specimens having to be placed in glass jars of various sizes, which are unwieldy and awkward to handle, especially in classrooms, and occupy a great deal of space in the museum.

As the specimens become old, or if exposed to the light, they soon lose their bright color. Various molds often grow in the final preserving fluid and destroy the specimen in that way. If one wishes to ship them elsewhere for exhibition purposes there is always the great danger of breaking.

In order to overcome these objections several workers have mounted museum specimens in "Kaiserling jelly"

in Petri dishes cemented to plate glass squares, the "Kaiserling jelly" being made by adding from 10 to 18 per cent. of the best grade of gelatin to the Kaiserling preserving fluid.

The pioneer and probably the most successful workers with this method in this country are Watters,[1] Coplin,[2] Albert,[3] Watters.[4] Specimens mounted in this manner are easy to handle, stand shipping well and occupy but little space. They have this disadvantage, however, that the gelatin is not clear water white and becomes darker with age, and is liable to shrink either from the glass or the specimen. This, of course, detracts very materially from the appearance of the specimen.

About fifteen or twenty years ago a method for mounting museum specimens in Kaiserling's fluid between watch glasses and plain glass squares was perfected in Germany. This method has been kept a profound secret by those who perfected it. These preparations are bound in a cardboard frame covered with book-cloth, and are very neat in appearance and durable. Several years ago the writer had the pleasure of examining some of the German specimens and also some that had been prepared in Kaiserling jelly, and was at once impressed with the beautiful appearance of the former, as they contained no air bubbles and the fluid was clear and contained no color; also that the cardboard case protected the glass background from being soiled when handled. I began at once experimenting in various ways to prepare mounts in Kaiserling fluid, as it appeared to me that it was much superior to any of the various other fluids. After many attempts, I succeeded in mounting specimens under watch glasses in Kaiserling fluid. These mounts retain their color and show relations well, are easy to handle and occupy a very small amount of space, and are permanent. The greatest difficulty experienced was to find an adhesive substance that would seal the watch glass to the glass square, which possessed sufficient elasticity to compen-

1. Watters: New York Med. Jour., Aug. 23, 1902, lxxvi, 318.
2. Coplin: Jour. A. M. A., Aug. 13, 1904, xxxxiii, 441.
3. Albert: Jour. A. M. A., June 30, 1906, xxxxvi, 1993.
4. Watters: Med. Rec., Dec. 22, 1906, lxx, 988.

sate for the expansion of the fluid during extreme changes of temperature without cracking and allowing some of the fluid to escape. Asphaltum with a melting point of about 230 F. was found to meet the above requirements. I have placed mounts cemented with this substance in an incubator at a temperature of 104 F. for forty-eight hours, and then exposed the same mounts to a temperature as low as 5 degrees below the freezing point for twelve hours without any undesired effects.

The method which I have adopted is as follows: The tissues selected for museum mounts are washed lightly in water to remove any blood or foreign matter that might adhere to them. If the specimen is a thick mass it is cut in slices about an inch in thickness and placed in Kaiserling's fluid No. 1 until fixed through, which requires from one to several days, depending on the size of the tissue and the amount of fluid used. It is best to use plenty of fluid. Care should be taken to place the specimen in the position that it is to assume when mounted. If this is neglected it is liable to become wrinkled and curled and can never be made to look well afterward. If it is desired to mount thin membranes, such as pleura, mesentery, peritoneum, etc., they should be stretched over glass frames before fixing, in order to prevent curling. Either glass or glazed earthenware jars should be used for fixing containers, as metal is liable to cause staining. As soon as the tissues are fixed through, they are washed in running water for fifteen or twenty minutes to remove as much of the formalin as possible from the surface. They are then trimmed down to the desired size and shape to fit into the watch glass, and placed in 60 per cent. alcohol until the color begins to return, then they are placed in 95 per cent. alcohol until the color is fully restored. This step must be watched closely, for if they remain too long in alcohol they fade again. As soon as the color is properly restored they are placed in Kaiserling's preserving fluid for a day or two and then mounted. It is always desirable to mount the specimens within a few days after fixing, in order to get the best results. Before mounting, the tissues are subjected to a partial vacuum of about 26 inches of mercury for from ten to thirty

minutes, depending on the tissue to remove imprisoned air and absorbed alcohol. If this is not done the alcohol which remains in the tissues produces fading.

Before using the watch glasses it is necessary to grind them perfectly level. This is done by sprinkling fine carborundum powder on a large piece of plate glass and then pouring a sufficient quantity of water on the powder to make it grind well. The grinding should be continued until the ground surface nearly equals the thickness of the glass. Watch glasses 6 inches in diameter are a very good size, but larger or smaller ones may be used, depending on the size of the specimen one wishes to mount. The glass squares should be made of plate glass 3/32 of an inch thick and 7⅞ inches square for the 6-inch watch glasses. The size of the square glasses should vary in proportion to the size of the watch glasses, if larger or smaller ones are used. Plate glass squares thicker than ¼ of an inch are undesirable, even for very large specimens requiring watch glasses 7½ inches in diameter. After the glasses are thoroughly cleaned, the specimen to be mounted is placed in the watch glass and covered with a glass square, allowing the watch glass to protrude far enough to form a lip. The fluid (Kaiserling's preserving fluid) is poured in at this opening until it runs over, then the watch glass is slipped toward the center sufficiently to close the opening and then set aside in a perpendicular plane to allow the air bubbles, if present, to rise, and then the process is repeated until no more bubbles rise, then moved to the center. If a number of mounts are to be made, the specimen and glasses may be immersed in a large quantity of fluid and put in place and taken out and set aside as before. If the watch glasses have been properly ground the glasses adhere so perfectly that the fluid does not escape. After all the bubbles have been removed, the mount is placed on a flat surface with the watch glass upward, and all moisture and greasy substances are carefully removed; then melted asphaltum, which has been heated to about 250 F., is poured around the joint between the two glasses. The amount of asphaltum should be liberal and should extend about ½ inch on the watch glass and an equal

distance on the plate glass. After the asphaltum has become cool and set, it can be trimmed with a knife and the surface smoothed down with a thick-bladed knife or other metal which has been heated to nearly a red heat. After the melted surface has again become cool, the mounts are set aside for a few days to determine if they have been perfectly prepared. If bubbles appear the specimen should be remounted, which is not a difficult task. The greater portion of asphaltum can be removed with a knife, and the remainder with xylol or gasoline, as it is very soluble in either of these fluids. If the specimen has remained perfect it can now be enclosed in the cardboard mounting. When 7⅞-inch glass squares and 6-inch watch glasses are used the cardboards should be 8 inches square, with a circular opening 5⅜ inches in diameter in the center. They should be about one-sixteenth of an inch thick and of good quality. The upper board should be covered on the top side with bookbinders' cloth, and on the under side it should have a piece of cardboard of the same size and thickness, with a circular opening 7 inches in diameter glued to it, thus allowing space for the asphaltum. The cloth should extend about an inch on all sides, allowing sufficient material to paste to the ends and under side. The lower board should be just 8 inches square with an opening the same size as the upper and covered with cloth in the same manner, only that the cloth does not project over the ends. A good quality of glue should be used to fasten the top and bottom cardboard securely to the glass and also for holding the cloth over the ends and to the bottom board.

Nearly all text-books pertaining to pathological technic give the formulae for Kaiserling's fluids, so I will not repeat them here.

The preserving fluid should be boiled for five or six minutes before using, and allowed to cool to about 80 F. This answers the double purpose of destroying mold spores and of driving off the most of the absorbed and imprisoned air in the fluid, thereby lessening the danger of bubble formation and subsequent growths of molds.

Feb. 9, 1914.

STUDY OF THE KIDNEYS OF RABBITS

EXPERIMENTALLY INOCULATED WITH STREPTOCOCCI AND OF THE KIDNEYS OF RABBITS TREATED WITH VACCINES AND ANTISTREPTOCOCCUS SERA

LEILA JACKSON AND E. R. LE COUNT

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In the course of animal experiments with streptococci carried out by Dr. D. J. Davis and Dr. J. J. Moore at St. Luke's Hospital, opportunity was afforded to examine the kidneys of 55 rabbits. These rabbits were injected with various strains of streptococci; 48 with streptococci producing lysis of red corpuscles when grown on blood media; 6 with streptococci isolated from cases of sore throat occurring during the milk-borne epidemic of sore throat of 1911 and 1912; and 1 with streptococcus viridans. Eleven of these rabbits received antistreptococcic serum either before or after inoculation with streptococci; 15 received vaccine before inoculation and 2 received both serum and vaccine.

The tissues were fixed in Zenker's fluid, imbedded in paraffin and stained with hematoxylin and eosin, phosphotungstic acid hematoxylin, polychrome methylene blue and eosin, also by the Giemsa and Wright methods for bacteria.

A number of writers have commented on the difficulties connected with the production of chronic nephritis in animals. Ophüls,[1] in his article, "Some interesting points in regard to experimental chronic nephritis," says, "a very serious obstacle to experiments of this kind is the spontaneous occurrence of chronic nephritis in the animals used. Even in rodents chronic nephritis does occasionally occur spontaneously." In the article on "Experimental cardio-renal disease,"[2] mention is made by Smith of his examination of the kidneys of fifty normal rabbits to control the results of experiments.

It is unfortunate that a more detailed account is not given by Smith of the condition in these kidneys, since

1. W. Ophüls: Jour. Med. Research, 1908, xiii, 497.
2. Christian, Smith and Walker: Arch. Int. Med., 1911, viii, 468.

we have so far been unable to find any other mention of the study of so considerable a number of normal rabbit kidneys. Smith's statements are limited to the following: "The lesions, when found, consisted in almost every instance of a single area of round cell infiltration, connective tissue increase or a small group of dilated tubules." He also remarks that "Some lesion is found in 11 of the 50 rabbits, or 20 per cent."

Inasmuch as in our series lesions were present in 88 per cent. of the animals, and 7 or 12 per cent. of the rabbits were without changes in the kidneys, it would seem, in view of Smith's results, that in about 68 per cent. of the rabbits the lesions might be due to streptococci.

The changes in the kidneys of rabbits inoculated with living streptococci without other treatment, and those receiving injections of killed streptococci or streptococcic serum or both, in addition to the injection of living organisms, are so alike that they may be described together. Some differences may be briefly referred to later.

In 7 of our series of 55 rabbits there were no changes in the sections examined. Acute changes were found in the kidneys of 15 rabbits and all but 2 of these occurred in rabbits dying within eleven days after inoculation. The other 2 were treated with antistreptococcic serum and died twenty-four and thirty-two days, respectively, after inoculation, and in each animal there was a mitral endocarditis.

Of the acute lesions, intracapillary bacterial emboli were most frequently encountered; they were found in the kidneys of 11 rabbits. In some animals these mycotic emboli occur in all parts of the kidneys, in others only in the glomerular loops or in the capillaries of the cortex or medulla; in a few cases there was necrosis of the surrounding tissue ordinarily without necrosis or cellular reaction. Abscesses were found in the kidneys of 2 rabbits, in one a 5-day rabbit, they were few and small and located in the medulla, in the other an 11-day rabbit, they were numerous and small, the largest about 0.2 mm. across, some partially coalescent, others fairly discrete, present in both cortex and medulla. Infarcts were found in the kidneys of 2

rabbits, and an acute glomerular nephritis in the kidneys of a rabbit dying seven days after injection. The lesions in the latter are characterized by large masses of cocci in the glomerular loops, hemorrhages into other glomeruli or into the capsular spaces with partially or totally disrupted blood-vessels, masses of fibrin and in some glomerular lesions a more or less cellular exudate.

Subacute changes, lymphocyte and plasma cell exudates were found more frequently than any other alteration, as early as the third day and as late as the 113th day. They were usually associated with other lesions either acute or chronic. We found them as the only change present in the kidneys of 9 rabbits, but associated with other changes in 23 rabbits. These exudates are in general small, varying in size from those containing 20 or 30 to those containing 100 or more cells, and located about blood-vessels, usually veins and most frequently around the arcuate vessels and vessels in the cortex. Less often they form rather large accumulations filling in defects in the parenchyma, some of them 2 mm. long by 0.5 mm. wide. They are composed almost exclusively of lymphocytes and plasma cells or a mixture of both, also large endothelioid cells are sometimes present in considerable numbers. Accumulations of plasma cells are somewhat less numerous than those of lymphocytes. In many of the kidneys in which there are exudates about blood-vessels there are in some of the veins more than the normal number of large and small lymphocytes and endothelioid cells. In these cells and also in the cells of the exudate surrounding the vessels mitotic nuclei are occasionally seen, and all stages of migration of these cells through the vessel wall may be observed.

Changes apparently of still longer duration were found in the kidneys of 22 rabbits. These changes were chiefly absence of parenchyma, dilated tubules and retention cysts, casts, scars and focal regenerative changes, most of them in animals killed or dying two weeks or more after inoculation. The focal regenerative changes referred to occur in the cortex and consist of dilated tubules lined with a low epithelium, sometimes empty, sometimes containing hyaline casts. The scars are usually wedge-shaped with the base at the

capsular margin producing pitting of the surface at that point and extending into the substance of the kidney for a variable distance, often the entire width of the cortex.

In this connection we may mention two instances of chronic nephritis occurring spontaneously in our series, one a chronic glomerular nephritis found in a rabbit dying eight days after inoculation, the other one in which numerous wedge-shaped scars and groups of dilated tubules were found in the kidneys of a rabbit vaccinated with killed streptococci; this rabbit was killed twenty-four hours after injection of living organisms.

Comparing the changes found in sections of the kidneys of rabbits treated with vaccine or serum and those receiving simply the injection of streptococci no particular difference as to the character of the lesion was observed, but in general the alterations were much fewer and milder in the treated than in the untreated animals.

No question can arise concerning the etiology of the acute lesions, streptococci being present in them, but as regards the subacute and chronic changes we must conclude that spontaneous nephritis was unusually prevalent in the animals from which we studied the kidneys or else, that in part at least, these more chronic changes were due to the experimentation used.

As already stated, we have been unable to find evidence for the occurrence of spontaneously developing changes in rabbit kidneys with a frequency comparable to that we found present in the animals injected with streptococci.

February 9, 1914.

PRELIMINARY NOTE ON THE ETIOLOGY OF ARTHRITIS DEFORMANS

E. C. ROSENOW

(From the Memorial Institute for Infectious Diseases, Chicago.)

The common presence of foci of infection, the history of previous infections, the occasional isolation of bacteria from the joints in chronic arthritis and the fixation

of complement by certain bacteria in arthritis deformans (Hastings) suggest strongly the infectious character of this disease. The similarity on the other hand, of the articular changes with those found in the nervous arthropathies, the associated dystrophies of the skin and nails, the symmetrical onset, the frequent involvement of nerve trunks and the exacerbations following nervous shocks are commonly cited as indicating a neurogenic origin. The chief objections to the infectious theory of arthritis deformans are that so many cases do not give a typical picture of infection and that no one thus far has isolated any organism from the tissues or joints in a considerable number of consecutive cases. Bacteriologic examination of the blood and of the articular exudate, when obtainable, usually has given negative results. It occurred to me that the lymph glands draining the involved joints would be a good place to look for organisms and this has been done in a considerable number of cases.

The glands are excised with strict aseptic precautions under local anesthesia and cultures made at once, a portion of the gland being reserved for microscopic study. The part used for cultures is dipped into boiling water or passed through a Bunsen flame so as to sterilize the surface, rapidly cooled in sterile salt solution, emulsified in a specially devised sterile air chamber[1] and inoculations made chiefly into tall columns of ascites-dextrose-agar. In this way organisms have been isolated from glands from all but three of thirty-eight cases of arthritis deformans, the duration of the disease ranging from two to seventeen years. Streptococci have been obtained in fourteen cases; a peculiar, streptococcus-like organism at first completely or partially anaerobic in nine cases; *B. Welchii* in nine cases, staphylococci in three; *Bacillus mucosus* in one case, and the gonococcus in one case. In a number of glands several organisms have been found at the same time. In no instance have the streptococci been hemolytic for human blood. They resemble on isolation the usual streptococcus viridans

1. The chamber in which this is done and the method of making the cultures is described in an article to appear in the Centralbl. f. Bakteriol.

more than hemolytic streptococci, although only three strains produced green on blood agar plates. There is often a marked difference between the type of organisms found, in foci of infection, such as the tonsil and of those found in the glands (or joints). All the streptococcal forms isolated have shown a marked preference for anaerobic conditions of growth in the primary culture.

Positive results have been repeatedly obtained from glands only 5 mm. in diameter. The number of colonies have ranged from 1 to 2,000. The virulence of all the strains tested has been slight; when first isolated the streptococci show a marked affinity for joints and muscles and in some cases the lesions would parallel closely the condition found in the patient from whom the strain was isolated.

In some cases the same organism has been isolated at the same time from more or less widely separated regions, e. g., epitrochlear and femoral glands, from gland and muscle; from gland, joint fluid or joint capsule (six cases). Often the size of the gland draining the joints is apparently proportional to the degree of articular involvement. There is often great sensitiveness of the patient to injections of killed organism (autogenous vaccine) isolated from the glands and marked improvement may follow such injection. These facts in conjunction with the affinity of the organisms for joints and muscles of dogs and intravenous injections would seem to leave little doubt but that the bacteria found in the glands draining the joints in arthritis deformans are the actual cause of the disease.

Microscopic sections of atrophic and often tender muscles and the thickened articular capsule in a number of these cases have shown a marked thickening and not infrequently a complete plugging of the blood-vessels, apparently not the result of organized thrombi, but rather of a primary endothelial proliferation. Bacteria have been found in areas of endothelial proliferation. In rabbits the exudate in the joints after intravenous injection and in the abdominal cavity after intraperitoneal injection usually shows a preponderance of endothelial cells. For these reasons the changes

observed in the blood-vessels about the infected joints may be regarded as primary rather than secondary, and it would seem as if in arthritis deformans the micro-organisms are taken up from the circulation by the endothelial cells which proliferate freely so that eventually the blood-supply is reduced or cut off, in consequence of which there result areas of lowered oxygen tension, diminished nutrition and atrophy. Such conditions would favor the growth of organisms which, on isolation, are sensitive to oxygen. Clumps of bacteria, some of which have been found to be alive, have been observed within thick layers of old fibrous tissue in the capsule of joints in which there was no sign of recent inflammatory reaction. It may be recalled that Axhausen was able to produce the gross and microscopic changes peculiar to arthritis deformans by ligating the blood-vessels supplying the structure of certain joints in dogs.

The details of these experiments will appear in *The Journal of Infectious Diseases.*

I wish to express my appreciation to Dr. Frank Billings for the opportunity to study many patients under his care and to the resident and attending staffs of the Presbyterian and Cook County hospitals and to the other physicians for their cooperation.

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SYPHILIS OF THE MENINGES*

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(From the Otho S. A. Sprague Institute and the Pathological Laboratory of Rush Medical College)

ABSTRACT

A report was made by Dr. Dewey of the examination of between fifty and sixty brains with changes in the meninges, some of them obviously syphilitic because of the definitely gummatous nature of the discrete masses of granulation tissue, others more cicatrized supposed also to be syphilitic because of their almost exclusive occurrence in bodies with changes, such as syphilitic scars in the capsule of the liver, gummas of the liver or spleen, syphilis of the aorta, etc.

The interest of the study centered about a careful review of the evidence of various kinds for the origin of the scars in the meninges in a syphilitic infection. In many instances definite gummas were found in deeper locations in the brain, usually minute and frequently in the deepest parts of the sulci about the fossa sylvii or in the cortex of the brain about such sulci, associated with the superficial scars which, as stated, first excited interest on account of their being encountered only in brains of bodies with indications of a syphilitic infection in other parts of the body. These scars, called "arachnoid scars" by Drs. LeCount and Dewey, are frequently lozenge shaped, located in the outer parts of the arachnoid membrane, and in the older

* A statement somewhat similar to this was made by Dr. LeCount at the meeting of the American Association of Pathologists and Bacteriologists in Washington, D. C., May, 1913.

lesions of this sort necrotic centers were frequently found surrounded by heavy bands of collagenous connective tissue resembling those characteristic of keloids. The scars were found most commonly stretched across the mouth of a sulcus.

In addition to the association of these scars with syphilitic lesions still other focal changes in the meninges were found which were not so thoroughly cicatrized, transitional alterations and these, too, associated not only with gummas of the brain and syphilitic lesions elsewhere in the body, but also with the scars of the arachnoid. Some corroboration was also obtained from tests made by Drs. Moody and Jackson of the blood and cerebrospinal fluid, the Wassermann reaction or the color reactions with colloidal solutions of gold known as Lange's test.

The observations on the whole were that scars in these meninges, arachnoid and pia, might be used in post-mortem examinations as evidence of a syphilitic infection in much the same way as the stellate scars in the capsule of the liver so universally regarded by those versed in pathologic anatomy as syphilitic.

Among the brains studied there were several with the rather unusual hyperplastic or nodular gummatous meningitis. Although the clinical histories were not as full as might be desired since the greater part of the material accrued from post-mortem examinations made to ascertain the cause of death, so-called "coroner's cases," no reasons developed for believing that any considerable number of the persons had paretic dementia. In ten instances death was sudden and unexpected.

One feature of the study of more than ordinary interest is that the alterations found in the meninges were usually on the vertex, whereas the usual accounts of syphilis of the meninges refer to it as a basilar meningitis.

December 8, 1913.

RETRO-AORTIC LEFT RENAL VEINS*

Frank Nuzum

(From the Pathological Laboratory of Rush Medical College)

In a considerable search through medical literature I have succeeded in finding only sixteen instances reported of the passage of the left renal vein behind the aorta.

The complicated development of the inferior vena cava is responsible for the numerous anomalies of the abdominal veins, since four of the veins present at varying stages of embryonal life take part in its formation. In dealing with anomalies of the renal veins, and particularly the left renal vein, we have to do with vestiges of the original post-cardinal channels. The instances in which a left renal vein passes behind the aorta, or is represented by one or more branches passing behind the aorta, are results of primitive anastomoses between these embryonal channels, the post-renal veins, which persist instead of atrophying as they normally do.

That anastomoses do exist between these post-renal veins during embryonal development has been definitely shown by Davis[1] who found as many as seventeen cross branches between the post-cardinals at one time during their development.

We believe that post-aortic left renal veins persist rather frequently throughout adult life and that the condition is not as infrequent as one might be led to believe by the small number of reported cases.

In the files of the pathologic laboratory of Rush Medical College are records of ten instances of post-aortic left renal veins. In six of these the left kidney is drained by a single vein which passes to the right and downward behind the aorta, emptying into the inferior vena cava at a considerably lower plane than the mouth of the right renal vein.

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* This article, somewhat more extensively written and with illustrations, may be found in Journ. Am. Med. Assn., April 18, 1914, pp. 1238-1241.

1. Davis, D. M.: On the Origin of the Vena Cava, Am. Jour. Anat., x, 461.

In one instance, two veins passing from the hilus of the left kidney unite and pass downward behind the aorta to empty into the inferior cava. An eighth specimen is somewhat similar, but here a single vein passing from the hilus of the left kidney divides into two vessels, both of which empty into the cava behind the aorta.

The ninth example has three branches springing from one main left renal vein, two of these passing behind the aorta and one anterior to it.

The final specimen has a persistent left postcardinal vein, and as this is of very infrequent occurrence, it merits a more careful description. A single vein passes from the hilus of the left kidney toward the right for a distance of 3.5 cm., when it divides into two branches, the superior and smaller of which passes horizontally behind the aorta, emptying into the vena cava 1.8 cm. below the mouth of the right renal vein; the inferior branch passes downward a distance of 2 cm. from the point of bifurcation, then turning to the right passes behind the aorta and ends in the cava 4.5 cm. below the point of entry of the right renal vein. The left suprarenal vein, according to Hochstetter, the remnant of the left subcardinal, empties into the left renal vein just before its bifurcation. The left spermatic vein empties into the inferior branch just after its division. One centimeter below the point of entry of the spermatic vein, a large vein lying just to the left of the spinal column and parallel with it also empties into the descending portion of the inferior, posterior branch. The vein originates from the left common iliac vein, which in this case is double, one part continuing on and joining the right common iliac to form the inferior cava, while the other at a point 6 cm. from the point of fusion of the two common iliacs turns upward on the left side of the vertebral column emptying, as before stated, into the inferior, posterior left renal vein. There is a small anastomosing branch between the two left iliac veins at the point at which the one turns upward to join the left renal vein. There is a second anastomosing branch between this left ascending branch and the inferior

cava, which is horizontal in direction, lies behind the aorta and is 3 cm. below the level of the inferior, posterior left renal vein.

Current explanations for orthostatic albuminuria are concerned with interference with the circulation of the kidneys. It seems reasonable to believe that the abdominal viscera falling to the sides of an individual on his back and deriving their blood supply from the aorta would exert tension on the branches of the aorta which supply them and pull the aorta closer to the spinal column. This would, in case of a post-aortic, left renal vein, compress the vein and interfere with the return of venous blood from the kidney. It is possible that the hyperemia produced might be responsible for the albuminuria, which is called hypostatic and observed following lying prone, disappearing when the erect position has been maintained some time.

January 12, 1914.

THE ORIGIN AND NATURE OF FETAL MOVEMENTS

Evarts A. Graham

(From the Otho S. A. Sprague Memorial Institute Laboratory of Clinical Research, Rush Medical College, Chicago)

Asphyxia of the fetus of sufficient grade will result in the production of fetal movements, more or less severe. The movements thus produced vary from mere attempts at respiration, sometimes resembling the fetal hiccup of Mermann, to more general muscular contractions, simulating the general convulsions of carbon-dioxid poisoning seen in the adult. At times these are sufficiently violent to be seen through the abdominal wall as distinct shocks. All of the generally recognized varieties of fetal movements, except those concerned with swallowing and sucking, have been produced experimentally by methods which induced an asphyxia of the fetus. The intra-uterine respiratory efforts are not accompanied by an aspira-

tion of any appreciable quantity of fluid into the lungs, and hence are not incompatible with life after birth. The explanation of this is not clear, but probably the contact of the skin with the air is an important factor in opening up the respiratory passages. The hypothetical intra-uterine rhythmical respiratory movements of Ahlfeld (physiologische intra-uterine Atmungsbewegungen) were not observed. The suggestion is made that the various active movements of the fetus experienced by many pregnant women in the latter part of pregnancy are expressions of a more or less severe, but usually transient, asphyxia of the fetus.

January 12, 1914.

IMMUNOLOGIC STUDIES IN EXPERIMENTAL STREPTOCOCCAL INFECTIONS

J. J. Moore

(From the Otho S. A. Sprague Memorial Institute and the Pathological Laboratory of St. Luke's Hospital, Chicago.)

In a paper previously reported before this society, the results of the curative and prophylactic treatment of experimental streptococcal arthritis with a concentrated anti-streptococcic serum were detailed. In these experiments four series of rabbits were treated with this serum: (a) after the appearance of acute arthritis; (b) immediately after receiving the living streptococci; (c) before the injection of the live streptococci; and (d) before and again after the injection of the live streptococci.

In none of these groups did the concentrated anti-streptococcic serum appear to have any preventative or curative effect on the acute arthritis. The opsonins were not increased, the weight of the animals remained the same and death occurred at an even shorter interval after the injection of the living streptococcus in the treated rabbits than in the controls. At the same time four cases diagnosed as chronic arthritis were treated with serum with no happy effects which could be directly traced to it.

The same concentrated serum combined with autogenous vaccines was employed by Billings and Nichol in the treatment of a large series of chronic arthritides with favorable effects. The results led us to try the effects of vaccines alone both on the patients and on animals. Of the four patients treated with vaccines after stopping the serum, three showed but slight improvement; this may be attributed to proper hygienic measures and to rest therapy. The fourth individual who had received serum over a period of two months without apparent benefit was entirely well a month after commencing the autogenous vaccine therapy.

Our object in the animal experiments was to produce an immunity in rabbits by prophylactic injections of a homologous streptococcic vaccine, to ascertain the degree and duration of that immunity, and incidentally the nature of the immunity.

TECHNIC

Rabbits were injected with five or six doses of a homologous vaccine, that is, the vaccine was prepared from the same organism which later was injected to produce the arthritis, at intervals of from two to four days. The injections were made subcutaneously on either side of the vertebral column. The first dose of vaccine was 500 million, and these were gradually increased so that the last one contained from one to two billion streptococci. Three or four days after the last vaccine treatment, the rabbits were injected intravenously with one-tenth of the twenty-four-hour growth on a blood-agar slant of the same organism, streptococcus (256). This amount of living streptococcus (256) had been shown by previous experiments to produce an acute arthritis in 95 per cent. of rabbits within four days, the other 5 per cent. dying of septicemia before that time. Suitable controls were made in all cases.

The vaccine was prepared in the following manner: The twenty-four-hour growth of the streptococcus on blood-agar slants was washed off with sterile normal salt solution, the large clumps broken up and then standardized in the customary method. The

emulsion was then heated at 60 C. for one hour and tested as to its sterility, enough phenol added to make a 0.5 per cent. solution and the vaccine preserved in the ice-chest. Suitable doses were then taken as required.

Of fifteen rabbits treated with prophylactic injections of vaccine, five or 33 per cent., were chloroformed on the first, fourth, ninth, tenth and twelfth days, respectfully, to complete a series of pathologic studies. Of the ten remaining, two died of the acute infection, one on the fourth day and the other on the ninth day. The other eight, or 53 per cent. of the total number, lived for varying periods of from one to six months, an average of three months and, unfortunately, died of the epidemic type of rabbit pneumonia before the duration of the immunity could be determined.

If we limit our figures to those which died from natural causes, we have eight out of ten, or almost 80 per cent., of recoveries. These figures are significant when compared with the recoveries in the serum and control groups. One, or 6.6 per cent., of the fifteen rabbits treated with serum recovered; one, or 9 per cent., of the eleven control animals recovered. A decided protection was therefore given by the vaccine.

Two rabbits were treated with vaccine after the injection of the living organism. Rabbit 26 received a dose of two billion on the third day and was found dead on the fourth before the appearance of any arthritis. Rabbit 32 received fifty million on the fourth day before the appearance of any joint involvement. On the morning of the fifth day the left shoulder was swollen. On the seventh and tenth days, vaccine in one billion doses was given with complete recovery by two months. The large dose of dead organisms in the first case may have brought about the rapid death and, in the second may have caused the joint involvement. However, we cannot state anything positive on these few results.

In the serum and control groups, in all cases, the animals had an acute arthritis or died of septicemia, and all gave symptoms of being sick, after receiving the living streptococci. On the contrary, two of the

vaccine-treated rabbits did not show symptoms of being sick and had no joint involvement. Rabbit 27 received a second injection of living streptococci (256) one month after the first and died in three days from abortion and septicemia. Rabbit 28 was injected twice, the injections being forty days apart; no arthritis or other symptoms appeared after either inoculation. While keeping this animal to test the length of the immunity it died from "rabbit pneumonia."

The average number of joints involved per rabbit in each series is as follows: Controls, 2.4; serum, 2.6, and vaccine, 1.3. The average number of days after the injection of the living streptococcus that joints appear is: Control, 2.5; serum, 3.5, and vaccine, 4. The latter figures do not include Rabbits 27 and 28 mentioned in the preceding paragraph. Thus the vaccine not only lengthens the interval of incubation, but aids in that a milder form of arthritis is produced and a less number of joints are involved.

We employed as a clinical standard of immunity the production of acute arthritis, since this produces symptoms which can be easily recognized in the living animal. A feature equally interesting, which, however, we did not observe until the animals came to autopsy, was the production of endocarditis. Hemorrhages and vegetations on the mitral valves were most common although the tricuspid and aortic valves and the lining of the left ventricle were quite frequently involved. We found endocarditis in 50 per cent. of the controls, 60 per cent. of those treated with serum, and in only 13.3 per cent. of those treated with vaccine.

Since eight of the rabbits lived more than one month, it may be said that these may have had an endocarditis and recovered, but of eight[1] dying within a period of twelve days after receiving the living cocci, only two showed heart lesions. This is 25 per cent., or less than half that shown in the other groups. Of other pathologic changes, Drs. Jackson and LeCount[2]

1. Rabbit 27, which died four days after receiving the second dose of living streptococci (256), is included in this number.
2. Jackson and Le Count: Tr. Chicago Path. Soc., February, 1914.

found that acute inflammatory lesions occurred much less frequently in the rabbits treated with serum and vaccine than in the controls.

The reactions produced in the animals by the vaccine and by the injection of living cocci produce the following curves. The temperature curves show no sharp changes after the vaccine injections, but in all cases there is a rise from 105 to 106 h. after the living cocci. This falls to practically normal within twelve days. The leukocyte count is also variable. It presents nothing distinctive before the live cocci have been injected after which there is a sharp rise to eighteen to twenty-two thousand; it then recedes and reaches normal by the eighteenth to the twentieth day. An important curve is that of the weight which in the case of the vaccine treated animals remained stationary or showed a gradual increase during the entire period. In the cases of the serum and control rabbits there was a rapid fall in weight in all instances after the introduction of the living cocci, but this did not occur in the vaccine group except in a few rabbits. In this group there is but a very slight decrease in weight, which soon returns to the normal.

The opsonins increase during the prophylactic treatment, fall after the live cocci are injected but soon return to above the normal. It would seem, therefore, that the immunity is very intimately associated with and probably dependent on the production of opsonins.

In summarizing, we may say that we have produced an immunity in rabbits by the prophylactic injection of a homologous streptococci vaccine which, measured by the clinical phenomena of acute arthritis, varies in degree. This probably to some extent depends on the individual animal. The duration of that immunity was apparently complete in one case over forty days. The immunity appeared to be associated with an increase in opsonins.

February 9, 1914.

DIAGNOSIS OF SYPHILIS BY TESTING FLUIDS FROM DEAD BODIES

A. M. Moody, Leila Jackson and E. R. LeCount.

(From the Laboratories of the Presbyterian and St. Luke's Hospitals)

Because of the frequency with which one of us during the course of post-mortem examinations encountered changes, possibly of a syphilitic nature, blood from the heart or large blood-vessels and cerebrospinal fluid were taken for the Wassermann test, and the last-mentioned fluid for the Lange colloidal-gold test to see if by this means the existence of a syphilitic infection might be demonstrated.

Luksch[1] in 1910, stated that the occurrence of the Wassermann reaction shortly before or after death, in his opinion, did not have much value on account of the changes in the blood serum produced by serious disease causing the phenomenon of complement fixation in a manner quite like syphilis. He observed such changes as the result of sepsis, uremia, pneumonia, even with recovery, and believes they may develop some time before death.

His results and those recorded by others[2] are grouped together in Table 1:

TABLE 1

Observers	No. Cases	Positive	Per Cent.
Bruck	101	59	58.4
Seligman and Blume	100	28	28
Schlimpert	361	46	18.7
Luksch	309	145	46
Simmonds	160	33	21
Lubarsch	262	55	21
Löhlein	149	42	28.2
Veszpremi	100	46	46
Krefting	115	43	37
Nauwerck and Weichert	206	57	28
Grüber	300	101	30
Total	2,163	655	

The above table consists only of series of blood examinations of serum removed from bodies coming

1. Luksch: Verhandl. d. path. Gesellsch., 1910, xiv, 245.

2. Bruck: Die Serodiagnose der Syphilis, Berlin, 1907. Seligman and Blume: Berl. klin. Wchnschr., 1909, xxiv, 116. Schlimpert: Verhandl. d. path. Gesellsch., 1909, xiii, 95. Luksch; Simmonds, ibid.; Lubarsch, ibid.; Löhlein, ibid.: Veszpremi Centralbl. f. allgem. Path. u. path. Anat., 1910, xxi, 193. Krefting: Deutsch. med. Wchnschr., 1910, viii, 366. Nauwerck and Weichert: München. med. Wchnschr., 1910, lvii, 2329. Grüber: Freidr. Bl. f. gerichtl. Medizin, 1912, lxiii, 81.

consecutively to autopsy regardless of the presence of clinical or anatomic signs of syphilis, that is, they do not concern selected material.

In the total number of 2,163 examinations, the Wassermann reaction was positive in 655, or 30 per cent. Mention is made in two instances of the results obtained by examining the blood obtained post-mortem from the bodies of persons possessing neither clinical nor anatomic evidences of syphilis, that is, the material *was* selected. One of these (Krefting) obtained twenty-four positive reactions from the blood of ninety-six bodies in which there was no syphilis clinically or anatomically. (26.1 per cent.) The other is the report by Simmonds[3] of twenty-four positive reactions in non-syphilitics as follows: nine sepsis; seven cachexia from phthisis and general carcinomatosis; three chronic pyelonephritis; two pneumonia.

The results of Candler and Mann (4) have not been included in Table 1 because of the somewhat different conditions, the patients being all inmates of an insane asylum. The reactions they obtained confirmed the clinical and anatomic diagnoses in 110 of 112 examinations of the spinal fluid, and eighty-six out of ninety-two examinations of the blood. The few instances where positive reactions were confidently expected and not obtained they refer to as percentages of "error" without, however, explaining the causes of error.

We have examined 190 fluids from dead bodies. Of this number 102 were spinal fluids, and 88 were blood serum [see Table 2].

TABLE 2.—RESULTS OF WASSERMANN-NOGUCHI SERUM TEST OF FLUIDS COLLECTED POST MORTEM

	POSITIVE		
	With Anat. Evidences of Lues	With No Anat. Evidences of Lues	Total
Cerebrospinal fluid	41	15	56
Blood	57	9	66
	NEGATIVE		
Cerebrospinal fluid	27	19	46
Blood	10	12	22

3. Simmonds: Verhandl. d. deutsch. path. Gesellsch., 1910, xiv, 251. Discussion of Luksch's paper.

4. Candler and Mann: Brit. Med. Jour., 1912, i, 537.

The Wassermann reaction was positive fifty-six times and negative forty-six times in the spinal fluids. This gives us 55 per cent. positives and 45 per cent. negatives. With forty-one, or 72 per cent. of the positive reactions, there were anatomical signs of syphilis and with fifteen, or 38 per cent., no signs of syphilis in the bodies.

Of the forty-six giving negative Wassermann with the spinal fluid, twenty-seven, or 58 per cent., came from bodies with syphilitic lesions. There were eighty-eight bloods examined, sixty-six, or 75 per cent. of which gave positive and twenty-two, or 25 per cent. gave negative Wassermann reactions. Of the sixty-six positive, fifty-seven, or 86 per cent. were from bodies in which signs of syphilis were present; only nine of the positive reactions were unaccompanied with anatomic evidences of lues. The combined results of the Wassermann reactions on the 190 examinations were 122, or 64 per cent. positive and sixty-six, or 26 per cent. negative.

Of the 122, or 64 per cent. positive cases, ninety-eight had anatomically syphilitic lesions while twenty-four (12.8 per cent.) had no anatomic evidences of lues.

Of the fluids from sixty-eight bodies which gave no reactions for syphilis, thirty-seven came from bodies with anatomic changes regarded as syphilitic and thirty-one from bodies with no such changes. The former number, thirty-seven, is equivalent to 19.4 per cent. of the total.

The twenty-four positive reactions obtained with fluids from bodies with no gross evidences of syphilis, equivalent to 2.8 per cent. of the 190 examinations, concerned deaths from the following:

Delirium tremens and bronchopneumonia	5
Cerebral hemorrhage	4
Uremia	3
Tumor	3
Ascending infection of urinary tract	2
Cirrhosis of liver with icterus	2
Peritonitis	1
Miliary tuberculosis	1
Diabetic coma	1
Chronic heart disease	2
Total	24

The Lange[5] gold test was used in testing fifty-seven of the spinal fluids. Eighteen of these gave reactions located in the region for the reaction regarded as positive for syphilis. Of these eighteen, only two were from bodies with no anatomic signs of syphilis. However, with one of these, there was a clinical diagnosis of tabes. In the other instance death was caused by poisoning. The thirty-nine remaining tests were modified by the presence of contaminating and non-luetic substances in the fluids, or gave reactions characteristic for lesions other than syphilis found anatomically, e. g., tuberculous meningitis.

The tests used in these examinations have been for the most part the Wassermann-Noguchi (human-rabbit) serum test; about one-fifth of the fluids were examined by the chicken-rabbit system (Dr. Jackson) and a few of the spinal fluids, as already stated, with Lange's colloidal gold reaction.

Besides the 190 fluids mentioned in the foregoing, there were from forty-eight other bodies, fluids which gave absolutely no reaction. They were anticomplementary because of the presence of contaminating substances and in some instances syrupy from post-mortem changes. Some of these, although free from hemolysis, contained a proteid which would coagulate solidly when heated at 56 C. for 20 minutes.

The collection of spinal fluid with a sterile Pasteur pipet from the spinal canal or lymph-spaces in and about the brain, after the skull is opened and during or after removal of the brain, is difficult to carry out without the collection of some blood or blood-serum at the same time. Such traces of blood in the spinal fluid, we believe, in many instances, rendered the fluid anticomplementary, although the fluids were freed from corpuscles by centrifuging. Other fluids contained bacteria and a flocculent precipitate which modified the Wassermann reaction one way or another.

5. Lange: Zeit. f. Chem. u. Verwandte Gebiete., 1912, i, 44—78. Sippy and Moody. Tr. Am. Phys., 1913, p. 720.

CONCLUSION

It would seem fair to state that under certain conditions the Wassermann reaction in the fluids collected after death is of value. Where the blood or spinal fluids have remained in the dead bodies long enough for post-mortem changes to occur in them, then the results cannot be relied on. Finally, in individuals dying from acute infections the test is often positive in many instances independently of a syphilitic infection or its absence.

The Lange test we regard of great service to differentiate syphilis from other lesions of the cerebrospinal system in those cases where a clear spinal fluid uncontaminated with blood is obtained; otherwise it is valueless.

March 9, 1914.

SUDDEN DEATH FROM MALARIAL COMA

REPORT AND DEMONSTRATION OF PARASITES IN TISSUES

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(From the Pathological Laboratory of Rush Medical College, Chicago.)

Different writers on malaria have for a long time used the term "pernicious malaria," meaning a malignant form of the disease caused generally by the estivo-autumnal parasite. This does not imply that each case of estivo-autumnal fever is "pernicious," but refers to a severe and often fatal form of malaria, in much the same way as it is used in connection with anemia and icterus to signify severe forms of these diseases. The term "pernicious malaria" is used synonymously with "tropical pernicious malaria," often used by the older writers.

It also has been the custom of many writers to subdivide "pernicious malaria" clinically into *comatose, algid, hemorrhagic, eclamptic* and *pneumonia forms,* according to the symptoms presented.

I became interested in the comatose variety on account of an occurrence here in August, 1913.

An old man was found unconscious in the street and brought to a near-by hospital. He developed a high fever and convulsions which increased gradually in number and severity, and died in coma after forty-eight hours. By a blood-count there were 19,600 leukocytes; no changes were found in the urine. He remained unconscious until death and no history of his movements nor of his illness was obtained. At the time of the post-mortem examination, made by Dr. E. R. LeCount as Coroner's physician, a marked hyperplasia of the spleen and solitary lymph-nodes of the bowel, a peculiar bluish-gray pigmentation of the surfaces of the brain and bowel and of the substance of the liver, and a generalized slight icterus, were found. Material fixed in Zenker's fluid was given me to search for malarial parasites. The diagnosis of malaria was made largely by the color of the liver and brain and also by the absence of any other infection to account for the changes especially of the enlarged spleen which weighed 440 g.

In connection with this occurrence the question arose, "How often does malarial coma cause death, how often does it occur in this climate and what is its medicolegal importance?"

The large mortality from malaria in warm and tropical countries is well known and according to statements by Thayer,[1] Celli,[2] Rogers,[3] Schauffler[4] and others the comatose variety of pernicious malaria is not at all uncommon.

It was hoped that the vital statistics of such countries might contain statements regarding the frequency of death from the comatose variety of malaria. The examination I have made so far has thrown no light

1. Thayer, W. S.: Lectures on Malarial Fevers, New York, 1897. Lecture V, p. 145.
2. Celli, Angelo: Die Malaria nach den neusten Forschungen, Berlin, 1913, pp. 50-72.
3. Rogers, Leonard: Fevers in the Tropics, 1910, London, pp. 200-201.
4. Schauffler, Edward W.: Reference Handbook of the Medical Sciences, New York, 1902, v, 679.

on this point. Even such complete statistics as those published by the East Indian government, or the Malarial Commission of the Royal Society of London, or the Imperial Malarial Conference or the Statistiche Delle Cause Di Morte published by the Italian government, do not mention the comatose form at all. Since most of the publications do give mortality figures for death from "pernicious malaria," an effort was then made to learn the frequency of the comatose variety among the others which form, as already mentioned, varieties of "pernicious malaria." This, too, was found impossible, and some idea of the difficulties encountered are illustrated by the following.

The mortality figures for "pernicious malaria" vary widely. For example, Hehir[5] states that the 20 per cent. of all deaths in India contributed to "pernicious malaria" is a high rate, whereas Rogers[6] regards 25 per cent. a low figure. The older Indian writers, according to Hehir and Rogers, give 90 per cent., and in the statistics published in the *Indian Medical Gazette* of Calcutta, in discussing vital statistics in 1910, it is stated that for many years 85 per cent. of all deaths are due to malaria and plague. Many other instances could be cited. Thayer,[7] Henson,[8] Thayer and Hewetson,[9] Ewing,[10] Craig,[11] Crosse,[12] Manson,[13] Osler,[14] and most of the contributions to this subject examined recognize the comatose variety as the most common form of "pernicious malaria," but actual figures are not given. Jackson,[15] discussing the condition in the United States, states that to his knowledge only one-fourth of 1 per cent. of all patients with pernicious malaria fail to recover.

5. Hehir, P.: Prophylaxis of Malaria in India, Allahabad, 1910, p. 15.
6. Rogers: Loc cit.
7. Thayer: Loc cit., p. 148.
8. Henson, Graham Edward: Malaria, St. Louis, 1913, p. 116.
9. Thayer and Hewetson: Johns Hopkins Hosp. Rep., 1895, v, 61.
10. Ewing, James: Jour. Exp. Med., vi, 2.
11. Craig, Charles F.: The Malarial Fevers, New York, 1909, p. 216.
12. Crosse, William Henry: Malaria in West Africa, 1892, London, pp. 49-50.
13. Manson, Leonard: Brit. Med. Jour., 1894, ii, 1252-1306.
14. Osler, Sir William: Prin. Prac. Med., New York, 1912, p. 253.
15. Jackson, Thomas W.: Trop. Med., Philadelphia, 1907, p. 304.

In addition to the writers mentioned, Schauffler,[16] Scheube,[17] Mannaberg,[18] Craig,[19] Ruge,[20] Deaderick,[21] and Osler,[22] state that pernicious malaria is rare in temperate climates and also that its comatose variety is rare in such climates. According to Ewing,[23] persons sick with pernicious malaria in the temperate climates are usually infected in southern latitudes.

Still another unexpected development of this examination of the literature was learning that such works on legal medicine as Hofmann,[24] Schmidtmann,[25] Petersen, and Haines,[26] Draper,[27] Glaister,[28] Ewell,[29] Taylor,[30] whose books contain long and explicit chapters on the cause of sudden unexpected death, do not consider malarial coma.

The excellent articles by Eskridge[31] and Forsyth[32] on the differential diagnosis of coma, fail to mention malaria. It would go too far to discuss all the articles and statistics which were looked over. It suffices to say that the legal importance of sudden death due to malarial coma and its frequency have not found such a place in the literature as one would expect. To-day, where long distances are covered in a comparatively short time, an infection contracted in southern latitudes may easily end fatally in northern regions. Ma-

16. Schauffler, Edward W.: Loc cit., p. 679.
17. Scheube, B.: Die Krankheiten der Warmen Länder, Jena, 1910, p. 61.
18. Mannaberg, Julius: Malaria, Nothnagel's Encyclop. American edition, Philadelphia and London, 1905, p. 283.
19. Craig: Loc. cit., p. 216.
20. Ruge, Reinhold: Einführung in das Studium der Malaria Krankheiten, Jena, 1906, p. 151.
21. Deaderick, William H.: A Practical Study of Malaria, Philadelphia, 1909, p. 203.
22. Osler, Sir William: Loc. cit., p. 253.
23. Ewing, James: Loc. cit., p. 123.
24. Hofmann, E. R.: Lehr. d. Gericht. Med., Berlin, 1909.
25. Schmidtmann, A.: Handb. d. Gercht. Med., Berlin, 1909.
26. Petersen and Haines: Text-Book of Legal Medicine and Toxicology, Philadelphia, 1903.
27. Draper, F. W.: Text-Book of Legal Medicine, Philadelphia, 1905.
28. Glaister, J.: Text-Book of Medical Jurisprudence, Edinburgh, 1910.
29. Ewell, M. D.: Manual of Medical Jurisprudence, Boston, 1909.
30. Taylor, A. S.: The Principles and Practice of Medical Jurisprudence, London, 1910.
31. Eskridge, J. T.: Difficulties in the Causes of Coma, New York Med. Jour., 1898, p. 173.
32. Forsyth, D.: A Postgraduate Lecture in Coma and Its Differential Diagnosis, Brit. Med. Jour., London, 1912, i, 1060-63.

larial coma may simulate other diseases. Thayer[33] cites Bastianelli and Bignami who believe that in the malarial districts of Italy, death from malarial coma is often mistaken for sunstroke. Petersen[34] states that the symptomatology of this form may simulate any organic disease of the brain.

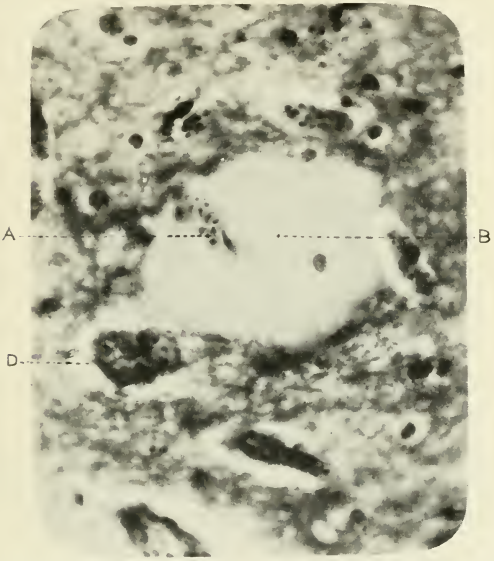

Fig. 1.—Small vessels of the brain blocked by malarial organisms (a and a') and malarial pigment, and surrounded by areas of necrosis (b) (450 diam.).

In Ewing's[35] contribution to the pathologic anatomy of malarial fevers the comatose type of "pernicious malaria" is divided into three pathologically and clinically distinct varieties: one due to the massing of

33. Thayer, W. T.: Loc. cit., p. 149.
34. Petersen, J. T.: Jour. Am. Med. Assn., 1913 li, 1807.
35. Ewing: Loc. cit., p. 119.

young ameboid parasites in the cerebral arteries, another to the embolic processes with temporary occlusion of the vessels in the small areas of the brain, and without uniform massing of parasites in the cerebral capillaries, and the third to the general toxemia of the infection. In the first of these the coma is rather slowly established in the course of the infection which is apparently connected with increase in size of the parasite and gradual filling of the vessels with thrombi of infected red cells, pigmented leukocytes and endothelial cells. Many young parasites are found in the

Fig. 2.—Young free estivo-autumnal malarial parasites in a brain capillary (1,200 diam.).

peripheral blood, the temperature is elevated, the reflexes absent and the patient passes usually from delirium into coma. Death occurs about forty-eight hours after the onset of the cerebral symptoms. In the second variety coma develops suddenly and may be as promptly recovered from. It is seldom fatal. There are extensive malarial lesions in the viscera, but few or no parasites in the brain. The distribution of parasites is otherwise uniform. In the third form coma develops slowly, except in cachectic cases, and is prolonged not being caused by massing of young parasites in the cerebral vessels. It is nearly always fatal.

The tissues I examined possess changes similar in all essentials to those described by Ewing as characteristic of the first of these three forms of coma. Sections imbedded in paraffin were stained with Wright's and Giemsa's blood stains.

The tissues of the brain are not changed except in the cortex where there are multiple, small, well-defined, circular regions of necrosis which almost invariably surround a capillary tightly filled with parasites (see Fig. 1). Otherwise the tissues stain well with all

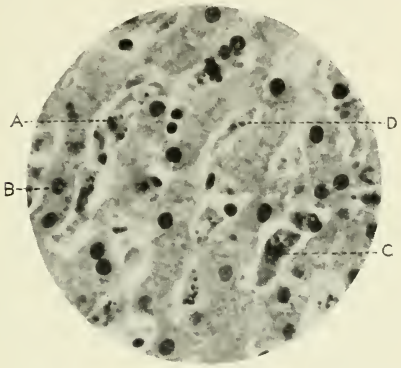

Fig. 3.—Liver. Note the absence of malarial organisms within the sinuses. The stellate cells of Kupffer (a and a') are of large size and heavily loaded with malarial pigment. The liver cells (b) are normal. The cell marked c is reproduced under higher magnification in Figure 4 (450 diam.).

of the stains employed. All of the capillaries of the white as well as the grey matter contain numerous young parasites, many of which are within red cells. The massing of red cells free and infected together with the free parasites gives to the capillaries a thrombosed appearance but no actual fibrin formation can be demonstrated (Fig. 1). The great abundance of parasites in the brain capillaries (Fig. 1 and 2) is in marked contrast with those of other organs. The endothelial cells lining those capillaries are greatly swollen and stain very deeply. Leukocytes are practically

absent. There are a few endothelial phagocytes present in the circulation. They are usually much swollen and heavily pigmented.

Exactly the reverse is true of the liver tissue. Here the parasites are very rare and phagocytosis of pigment conspicuous, the stellate cells of Kupffer being loaded with large pigment granules and swollen to several times their normal size (Fig. 3). Occasionally a partly digested parasite can be made out in these cells which suggests that the phagocytic cells did not take up the pigment granules only after the parasite

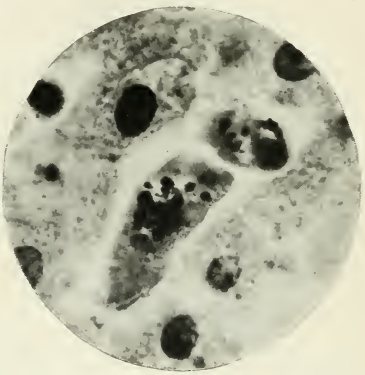

Fig. 4.—Large stellate cells of Kupffer (c of Fig. 3) containing malarial pigment and partially disintegrated organisms (1,200 diam.).

had been broken down in the blood-stream, but that the destruction of the parasite actually took place within the phagocytes (Fig. 4). The hepatic parenchyma is in general unchanged. Some of the cells surrounding the central (intralobular) veins have pyonotic nuclei. Few foci of fatty changes were observed. The connective tissue of the interlobular bands (portal canals) is frequently infiltrated with small mononuclear cells resembling lymphocytes.

The spleen contains large amounts of blood and there is a marked increase in parenchyma cells. Para-

sites of the type described are abundant both free and within erythrocytes (Fig. 5). Pigment is deposited in large endothelial cells scattered throughout the pulp. There are a few very small regions of necrosis in the pulp.

The alveoli of the lungs and the bronchi are filled with coarsely granular material typical of body fluids

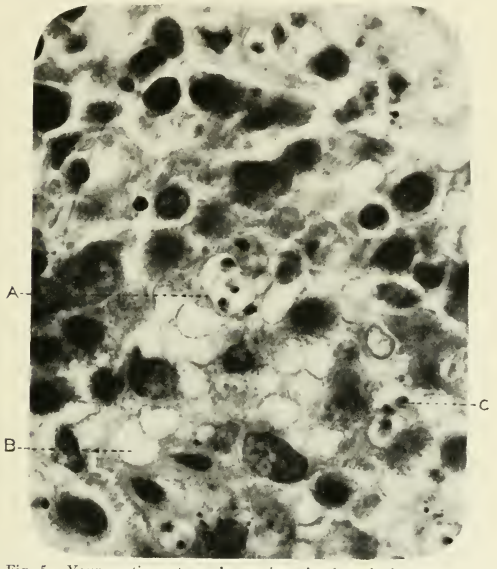

Fig. 5.—Young estivo-autumnal organisms in the splenic parenchyma: a, organisms within an erythrocyte; b, normal erythrocytes; c, free parasite (1,200 diam.).

as coagulated by hardening fluids. Cells with blood-pigment and other pigments judging by their color are present. The capillaries contain a fair number of parasites, the lung tissue does not stain as well as other tissues.

In the kidneys parasites are very scarce except in the large vessels. The tissue alterations are marked, the epithelium lining the convoluted tubules and loops of Henlee especially are in all stages of coagulation necrosis. The glomeruli are practically unchanged.

The tissues of the thyroid gland are not materially altered. Rows of parasites are present in the capillaries.

There is a marked accumulation of parasites in the capillaries of the myocardium. The muscle fibers have a fragmented appearance and contain a few pigment granules which have a green color with Wright's and Giemsa's stains. In the capillaries of the thyroid gland and the myocardium a few crescents occur.

This unequal distribution of parasites has been observed and commented on by several investigators. Barker[36] thought that the slow circulation and the caliber of the vessels were instrumental in producing it, but Ewing[37] found even in the different varieties of coma, that distribution varies greatly and also as might be expected in the different forms of malaria.

March 9, 1914.

SECONDARY AND EXTENSIVE INVOLVEMENT OF THE URETER WITH HYPERNEPHROMA

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W. A., 58 years of age, a watchman by occupation, suffered repeated attacks of renal colic during the past four years. The first attack came on suddenly with acute pain in the left lumbar region which radiated along the course of the left ureter and was associated with nausea and hematuria and followed by chills and fever. These attacks were precipitated by exposure, coughing, lifting or through straining during urination. They were very frequent and of varying intensity, only the severe ones being accompanied by hematuria. He enjoyed good health up to four years ago

36. Barker, L. F.: Johns Hopkins Hosp. Rep., 1895, v, 267.
37. Ewing: Loc. cit.

with exception of an attack of acute appendicitis seventeen years ago, for which he was operated. Two months after the first attack he was operated on again for "bladder stone" and after ten weeks' drainage the suprapubic vesical fistula closed. He was a very heavy drinker.

Oct. 20, 1913, he entered the Cook County Hospital to the service of Drs. Miller and Hamburger, suffering from acute renal colic. Examination revealed a fairly well-nourished, but somewhat anemic man past middle age, who seemed uncomfortable, but not actually ill. Anemia was apparent. There were coarse râles heard over the entire chest. There were no noteworthy changes found by examination of the heart; the systolic pressure was 125 mm. of mercury, the diastolic 77 mm. The abdomen was somewhat pendulous and thick walled. The liver could be felt a finger's breadth below the costal margin. There was an indefinitely palpable mass in the left flank which seemed to pass across the midline, slightly movable, firm, definitely nodular, and distinctly tender. The prostate gland was enlarged. Repeated examination of freshly voided urine revealed albumin, hyaline and granular casts and many epithelial cells. No tubercle bacilli were found. Analysis of a test meal revealed no free hydrochloric acid; the combined acidity was 10. Some long bacilli were found but there were no sarcinae and no occult blood. The blood contained 3,480,000 erythrocytes and 14,450 leukocytes, of which 13 per cent. were small mononuclears, 3 per cent. large mononuclears, 3 per cent. eosinophils and 81 per cent. polymorphonuclear neutrophils. It was impossible to get any definite information by radiographic examination. The patient suffered continual pain in the left loin, repeated chills with fever and vomiting, and on Jan. 10, 1914, died.

Anatomic Diagnosis.—Hypernephroma of the left kidney with extension into the left renal vein and down the left ureter to the bladder; left chronic suppurative pyelonephritis; fibrous adhesive perinephritis; adenoma of the right adrenal gland; right chronic diffuse nephritis (large white kidney); chronic indurative fibrous thickening of the aortic and mitral valves of the heart; hypertrophy of the myocardium with marked fatty changes; extensive hyperemia and moderate edema of both lungs; cloudy swelling of the liver and right kidney; hyperplasia of the spleen; healed encapsulated caseous and calcareous tuberculosis of the tracheobronchial lymph-nodes; ancient healed laparotomy scars; anemia; hypodermic needle puncture wounds of both arms.

"The left kidney, together with its adrenal gland measures 20 cm. in length, 14 cm. in width and 12 cm. in thickness; its weight is 1,080 gm. The upper pole is firm, the remainder of the kidney nodular and fluctuating. On incision approximately 500 c.c. of greenish thick pus escapes. The section reveals a well-circumscribed tumor mass occupying the upper third of the kidney and extending down the renal cortex to the lower pole. The tumor substance is mottled pink and gray and in the lower two-thirds the renal cortex can be distinguished as a thin band of tissue beneath the capsule. The central and pelvic portion of the kidney is made up of many thin-walled cavities filled with pus. The largest of these cavities is ovoid, measures 6 cm. in length, occupies the position of the renal pelvis and points downward and posteriorly very nearly through the renal cortex. In the center of the cavity is a mass of necrotic débris. The remaining smaller abscesses are disseminated throughout the lower two-thirds of the anterior half of the kidney. With the exception of a thin band of cortex, the renal parenchyma seems to be entirely displaced by tumor tissue or thin-walled abscesses."

The tumor of the left kidney possesses unmistakable histologic characteristics of a hypernephroma. It extended into the pelvis of the kidney and down the ureter—very nearly to the bladder—and also into the mouth of the left renal vein.

Careful examination failed to demonstrate any distant metastases. There was a secondary growth in one of the lateral lumbar lymph-nodes adjacent to the left kidney.

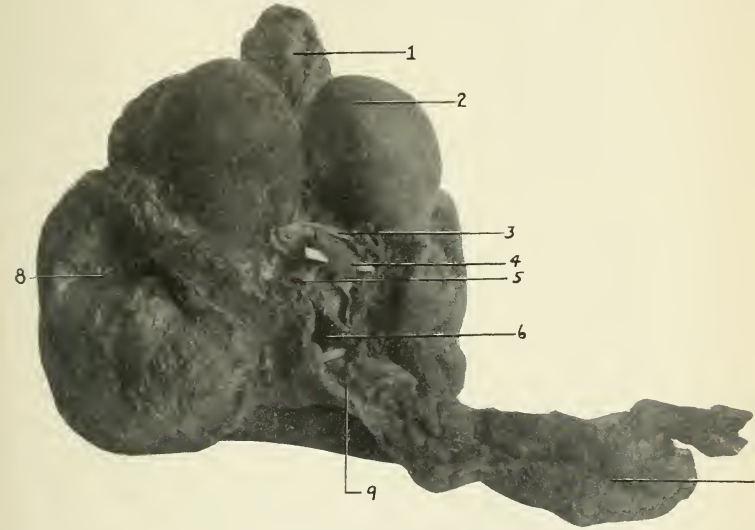
"The ureter is greatly distended, 2.5 cm. in diameter and its lining is made up of friable tumor tissue 1 cm. in thickness, corresponding in color and consistency to the adrenal tumor. The same tissue lines the pelvis of the kidney, is uniform in thickness throughout the pelvis and ureter and ends abruptly 1 cm. above the ureteral orifice of the urinary bladder."

A careful examination of microscopic preparations from a number of places in the ureter was made to see if there was any evidence of an extension from the ureter by lymph-channels in its wall.

The lymphatics of the ureter have been studied by a number of investigators. Sakata,[1] working under Von Mikulicz on the experimental study of ascending urinary infections, reviewed the literature of the

1. Sakata: Archiv. f. Anat. u. Physiol., 1903, pp. 1-12.

lymphatics of the ureter and after an exhaustive study of the ureters of the horse, ox, hog, sheep, dog and man, concluded that there are no demonstrable lymphatics in the mucosa and submucosa of the ureter, but that well-formed lymph-vessels, running parallel to the blood-vessels, are present in the muscular and outer coats. He found that those in the middle portion of the ureter drained into the lymph nodes behind the



Left Kidney with Hypernephroma Extending down the Ureter

1. Cut surface of hypernephroma. 2. Hypernephroma. 3. Renal vein. 4. Canalized hypernephroma in the renal vein. 5. Renal artery. 6. Renal pelvis. 7. Ureter lined with hypernephroma tissue. 8. Collapsed abscess wall. 9. Region of ureter in which hypernephroma cells have invaded the lymphatics.

aorta and along the course of the inferior vena cava; those of the lower segment of the ureter, (below the level at which the ureter crosses the common iliac vessels), into the hypogastric nodes, or they pass over into the efferent lymph-channels of the fundus of the bladder; from the upper segment of the ureter,

(above the level at which the spermatic (ovarian) artery crosses the ureter), the lymphatics pass into the regional lymph-nodes, which are of variable location, and some pass into the efferent lymph-streams of the kidney. The lymph-channel connections between the bladder and kidney, he believes are indirect, through the regional lymph-nodes and their connections, or through intervening lymph-connections in the ureter.

Gerota[2] found that the lymphatics of the bladder are confined to the muscular coat and that they anastomosed directly with the lymph-vessels of the ureter.

Stahr[3] in his study of the lymph-apparatus of the kidney, found three distinct networks: one in the cortical substance, one just beneath the capsule, and the third in the loose areolar tissue external to the capsule. The subcapsular network has numerous connections with both the cortical and subserous networks. The efferent vessels of the cortical layer follow the renal vessels through the medulla of the kidney to the hilus and emerge in several trunks which terminate in the lateral lumbar nodes situated along the course of the aorta and inferior vena cava. The efferents from the uppermost of these nodes pierce the crura of the diaphragm and enter the thoracic duct. The subcapsular plexus has no efferent vessels. The efferent vessels of the subserous plexus terminate in the upper lateral lumbar nodes independent of the efferent vessels from the cortex.

Bauereisen,[4] with special precautions against trauma, inoculated the urinary bladder of guinea-pigs with tubercle bacilli to produce, if possible, ascending tuberculosis of the urinary tract. He found that if the bladder mucosa was intact no infection occurred and that when the ureter was unobstructed, tubercle bacilli were found in the bladder but not in the ureter or pelvis of the kidney. He found also that if the ureter was occluded in any way, as a rule, ascending urinary tuberculous infection followed, whereas in long-standing cases of tuberculosis of the bladder the infection

2. Georta: Piersol, Human Anat., Philadelphia and London, 1907, 985.

3. Stahr: Archiv. f. Anat. u. Physiol., 1900, pp. 41-84.

4. Bauereisen: Ztschr. f. Urol., 1910, iv, 883-884.

travels to the mucosa of the ureter by anastomoses between the lymph-channels of the ureter and bladder.

In the microscopic preparations previously referred to from many places in the left ureter with the secondary growth of hypernephroma, the ureteral mucosa and submucosa is entirely destroyed and replaced by hypernephroma tissue and the muscular coat by fibrous tissue. In that portion of the ureteral wall corresponding to the muscular coat there are many blood-vessels, some of which are packed with red blood-corpuscles. Adjacent to these there are definitely outlined channels lined with endothelium and in sections taken from the upper portion of the ureter, these channels are distended with hypernephroma cells.

Beneath the outer coat of the ureter there are similar, but larger spaces packed with hypernephroma cells.

Because of their position in the muscular coat and their close relation to the blood-vessels, it seems reasonable to assume that these spaces, lined with endothelium and packed with hypernephroma cells, are lymph-vessels of the ureter. It is interesting to note that this hypernephroma has extended into the lymphatics of the ureter only in the upper portion—the oldest part of the process of extension. It will be recalled that the hypernephroma extends down to within 1 cm. of the bladder.

Because there is so little involvement in the lymph-nodes adjacent to the ureter, and because only in the uppermost, oldest portion of the tumor invasion of the ureter, is there demonstrable tumor tissue in lymph-channels, it seems highly probable that extension took place along the mucous membrane of the ureter, and after destruction of the mucosa and submucosa extension into the lymphatics of the muscle coat occurred.

In fact, no evidence was obtained from the examination of lymph-channels in other than the outer coats, and in this respect the opinions cited, especially those of Sakata and Bauereisen, are in a measure confirmed.

March 9, 1914.

DEFECTS OF THE PARIETAL PERICARDIUM

Angus L. Cameron

(From the Pathological Laboratory of the University of Chicago.)

Cases of defective structure of the parietal pericardium, in which the development of the heart is normal and in which this organ lies in its normal position inside the closed thoracic cavity, are extremely rare, very few cases having been reported in the literature. Peacock knew of only five such defects when he published his work on "Malformations of the Human Heart" (second edition) in 1866. In 1878 Faber was able to find in the literature the reports of only nine cases. He reports a case of his own, which makes a total of ten cases known to him. Among 13,000 necropsies performed at the Pathological Institute at Leipzig from January, 1900, until October, 1909, only two cases of defects of the pericardial wall were disclosed. I have found in the literature the reports of twenty-seven cases of defects of the parietal pericardium, and in fourteen of these cases I have had access to the original reports, the reports of the other thirteen cases having been found in connection with the above-mentioned original reports. I was unable to obtain the report of the case of A. Hewson.

The defect may be so great as to consist of a complete absence of the parietal pericardium or it may be so slight as to consist only of a small opening on the left side of the pericardial sac. Four cases of complete absence of the parietal pericardium have been reported. In most instances, however, the parietal pericardium is represented by rudimentary duplications or half-moon-shaped folds in varying degrees of development, which lie on the right side of the heart and which arise from different organs or structures to which the normal pericardium is attached. These rudiments, which are generally adherent inferiorly to the diaphragm, oftentimes form one or more pouches, which are lined with a normal serosa and which may enclose a portion or all of the right heart and less often a portion of the left heart, together with the right heart. In some cases the parietal pleura is con-

tinued from the great vessels of the heart, forming fringe-like projections and pouches which may enclose a portion of the heart. The visceral pericardium is generally normal. It may, however, be involved in fibrous adhesions and it may also show "soldier's spots." Fibrous adhesions involving the pleura, the surface of the heart, the pericardial rudiments, the diaphragm and the thoracic wall are common. Fibrous adhesions are present in a large majority of the cases.

In those cases in which the parietal pericardium is quite rudimentary the heart is often described as lying in a common cavity with the left lung. In only one such case was the heart described as lying between the two pleural cavities. (Cited from Faber.)

In reviewing the literature six cases were found which may be of special significance, the reason for which being disclosed later. The first of these cases is that of an anencephalic full-term child in which there was deficiency in the left side of the parietal pericardium, through which the left auricular appendix protruded, the opening being clearly a patent pleuro-pericardial foramen.

In the second case the heart was contained in a pericardial sac, on the left side of which there was an opening as big as the palm of the hand. The sac was attached to the diaphragm, and enclosed the inferior and right aspect of the heart from the base to the apex.

In the third case a large patency was present in the upper part of the pericardium, measuring ventrically 3½ inches and transversely 3 inches. The aorta from its first appearance and anteriorly to about an inch beyond the origin of the left subclavian artery was visible through this defect, as was also the beginning of the pulmonary artery. By means of the defect, the cavity of the pericardium communicated with that of the left pleura. It is interesting to note that only one kidney was present in this case and also that there was a septum in the urinary bladder.

Boxall reports a case in which a defect was present in the left side of the parietal pericardium through

which the heart had ruptured into the left pleural cavity.

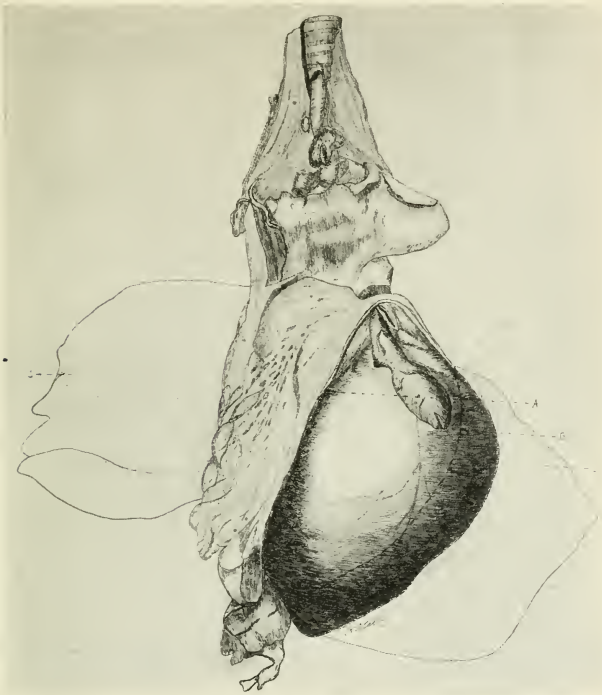
The fifth case is one of pneumothorax with congenital opening in the pericardium. "An opening in the pericardium, which contained some turbid fluid and air, was found to be situated at its upper part on the left side anterior to the pulmonary artery. It communicated with the left pleura above the root of the lung, but had no connection with the lung itself; oval in shape, one-eighth of an inch by one-eighth of an inch, its margin was perfectly smooth, presenting no appearance of erosion, but the appearance of a congenital opening."

The sixth case is one of a large pleuropericardial foramen. "The opening between the pericardial sacs appeared as an opening from 7 to 8 cm. in diameter. The edge was free throughout its course, which extended from above the pulmonary artery, thence over the root of the lung. From there it arched slightly forward, following the grove between the systemic and pulmonary aortae. At the junction of the pulmonary artery with the right ventricle the fold turned downward and backard, then upward, to terminate back of the left atrium. The free edge continued laterally to the left, forming the left parietal layer of the pericardium, and to the right, forming the right costal pleura. Through the opening could be seen the pulmonary artery and left auricular appendage. Aside from the large opening in it the pericardium was normal." Only a few adhesions were present over the apices of the lungs.

In none of the twenty-seven cases reviewed was the defect reported to have been diagnosed during life. Faber reports a case in which repeated physical examinations of the cardiac region during life led to no diagnosis of a defect of the pericardium, a condition which was revealed at autopsy.

The defect of the parietal pericardium reported in this paper was disclosed at necropsy in the case of a male laborer, a patient in the Cook County Hospital on the service of Drs. Tieken and Irons. Necropsy was performed four days after death by Dr. H. Gideon Wells. The patient was 67

years old, an alcoholic, and had died from bronchopneumonia, dilatation of the heart and chronic interstitial nephritis. A clinical diagnosis had been made of pulmonary



A—Anterior free border of pericardium. B—Posterior free border of pericardium. C—Diaphragm.

emphysema with bronchopneumonia. This partial error in diagnosis was due to a deformity of the chest, the cause of which follows. There was a history of a fall of 17 feet through a hatchway five years previous to death, at which

time numerous and profound injuries were sustained which rendered the person unable to do physical work.

A very sharp kyphosis occurred at about the eleventh and twelfth dorsal vertebrae. There was a compensatory lordosis at the sixth dorsal vertebra with exostosis close to the left of the vertebrae, also a severe right lateral scoliosis with some lordosis involving the lumbar vertebrae. The vertebral column was almost rigid, a little freedom for movement being present above the fifth dorsal vertebra. A decided ankylosis was present nearly throughout the column. Deformities involving the sixth and seventh ribs in the axillary space were present. A lateral flattening of the chest was present on the opposite side in the region of the right axilla. The second, third and fourth ribs were prominent anteriorly and the arching forward of the sternum was very marked. As a result the chest was full and voluminous and fixed as if in deep inspiration. This in part led to the faulty diagnosis of pulmonary emphysema. In addition to the above-described deformities, a conspicuous scar of fibrous tissue, extending across the entire width of the anterior surface of the right lobe of the liver was disclosed at necropsy. It extended into the liver substance 2 mm. and was adherent to the abdominal wall. This lesion, no doubt, was the result of the fall. There was also found in the aorta, just below the origin of the bronchial artery, a transverse fold 1 to 2 mm. thick, which involved all the three coats and extended two-thirds the distance around the vessel. It seemed to have been produced by inflammatory adhesions of the adventitia, but might have resulted from a folding of the aorta because of shortening due to the deformity in the vertebral column.

With the exception of an enlargement of the heart to the left and some heart murmurs and sounds, nothing abnormal had been found on physical examination of the cardiac region during life. It is quite probable that the dilatation may have been the result of the defect in the pericardium, for it has been shown, especially by Barnard, that the parietal pericardium has an important function in preventing dilatation of the heart.

On removal of the sternum dense fibrous adhesions were descried between it and the pericardial structure. On further examination it was found that the parietal pericardium was represented by only a pouch-like structure on the right and inferior aspect of the heart. The left side of the heart was entirely devoid of a parietal pericardial covering. The heart was greatly distended, chiefly transversely,

all of its chambers being involved. It lay free in the left thoracic cavity and there was a total absence of adhesions about it. It showed no signs of trauma. The pericardial sac was about one-half the size of the heart and could be made to contain all of the right auricle and about one-half of the right ventricle. The apex could not be forced into the pouch on account of the longitudinal enlargement of the heart, and therefore the cavity of the pouch could not be made to be completely occupied by the heart. This structure resembled closely a normal parietal pericardium through which a section had been made, passing just to the left of the pulmonary artery and missing its attachments to the diaphragm on the left side by a distance of about 2 cm., the plane of this section being at right angles to a vertical plane of the body. The pouch was formed for the most part by the development of the pericardium anteriorly and inferiorly. Posteriorly it was represented by a narrow band of tissue whose greatest width was 2 cm. and which became narrower as it ascended until, at its attachment to the pulmonary artery, it was merely a cord-like structure about 0.5 cm. wide and 2 mm. thick. The left free margin of this pouch was sharply defined except for a distance of about 7 cm. on the left inferior margin where a flap of thin fibrous tissue, heavily laden with fat, was prolonged and lay free on the diaphragm. Inferiorly and posteriorly this flap was continuous with the pericardial sac. The fibrous pericardium was normal, save for several marked prolongations of fibrous tissue, heavily laden with fat, which were present on its anterior aspect. The serous lining of the pouch was normal throughout. The general character of the condition is shown in the accompanying illustration, for which I am indebted to H. A. Callis.

In all the twenty-seven cases which I found in the literature the anomaly of the parietal pericardium is described as being congenital. In this case, however, a complicating factor enters in, namely, the fall of 17 feet, which renders a positive conclusion difficult. There is the possibility that this anomaly was congenital. The fact that there was a total absence of adhesions about the heart and also that, with the exception of the fold in the aorta, neither the heart nor its great vessels showed any signs of trauma, are significant factors in support of this view. It would seem, however, to be a rather remarkable coincidence that a con-

genital anomaly of this kind should occur in the case of a person who had through injury suffered such severe deformity of the other parts of the body in close relation to the heart.

There is also the possibility that this anomaly was in part congenital and in part due to injury. There may have been a congenital opening in the pericardium similar to the six cases previously described through which, at the time of the accident, the heart was ruptured into the left thoracic cavity. This condition of affairs would likewise be a remarkable coincidence.

The heart may have been ruptured through a comparatively normal pericardium. In support of the view that the anomaly was in part, at least, acquired is the significant fact (previously noted) concerning the fold in the aorta; also, the presence of adhesions between the sternum and the mediastinal tissues. This finding points to the probability that the heart and the parietal pericardium were seriously involved at the time of the reported accident, especially when one at the same time considers the other numerous and profound injuries which are known to have been due to the accident and also the extreme rarity of congenital defects of the parietal pericardium. On the other hand, the lack of other adhesions, and especially the free, rounded fatty margin of the remaining pericardial folds, make it impossible to conclude that the defect is not congenital.

April 13, 1914.

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THE COMPARATIVE PHYSIOLOGY OF PURINE METABOLISM*

H. Gideon Wells and George T. Caldwell

(From the Pathological Laboratory, University of Chicago.)

Previous studies have shown that the human organism contains no enzymes which will destroy uric acid *in vitro,* in which respect man differs from all other mammals hitherto investigated. This corresponds with the repeated observations, especially of Wiechowski, that man alone of all domestic mammals excretes uric acid rather than allantoin as the chief end-product of purine metabolism. These facts have been especially emphasized of late by Andrew Hunter. One of us found that even the monkey has no demonstrable uricolytic enzymes in its tissues. Wiechowski made the interesting observation that the chimpanzee, like man, excretes only uric acid and little or no allantoin, while Hunter and Givens reported that monkeys resembled the other mammals in excreting chiefly allantoin, corresponding with our observations on the purine enzymes of the monkey. We have recently, through the kindness of Dr. W. T. Hornaday of the New York Zoological Society, come into possession of two fresh bodies of anthropoids, a male chimpanzee and a female orang-utan. Examination of their tissues shows that, like man, they do not possess the uricolytic enzyme, uricase, demonstrable *in vitro.* They also resemble adult man in having guanase but no demonstrable adenase. Hence it seems that the anthropoids stand with man in constituting, in respect to uricolytic power, an exception to all other known mammals; the monkeys resemble the other lower mammals in possess-

* The details of this work will be published in the *Journal of Biological Chemistry.*

ing uricase, and hence in this property the anthropoids stand closer to man than to the monkeys, as they are also said to do in serologic reactions. We have found a marsupial, the opossum, to have uricase, xanthine-oxidase, guanase but no adenase. In respect to uric-acid destruction our results agree perfectly with the urinary analyses of Hunter and others.

April 13, 1914.

PRIMARY CARCINOMA OF THE BRONCHUS WITH PREGNANCY

Carl H. Davis

(From the Clinic of Professor Webster, and the Pathological Laboratory of Rush Medical College.)

Primary carcinoma of the bronchus is apparently a rare condition. In a recent study Weller[1] collected eighty-nine authentic cases and reported another. The sex is given in eighty-seven cases in this collection of which seventy were males and seventeen females. Three cases are recorded in the autopsy records of Rush Medical College, two cases in males having been reported by Drs. Davis and LeCount.[2]

The present case is of considerable interest, in that the carcinoma was here a complication of pregnancy. Death was due to pulmonary embolism, the emboli evidently coming from thrombi in the uterine veins.

Mrs. A., aged 34, entered the Presbyterian Hospital on the service of Professor Webster in May, 1910. She had been married six years, had two healthy children and one miscarriage. Midwives had confined her each time, but in this pregnancy the visiting nurses persuaded her to try the hospital, as she was too weak to do anything at home. She stated that there had been some nausea and vomiting, but that her most distressing symptom was pain in the left chest. This pain began a short time before she knew of the pregnancy and had gradually increased in severity until at the time she entered the hospital it was constant and so severe that she could hardly sleep.

1. Weller, C. V.: Arch. Int. Med., 1913, ii, 314.
2. Davis and Le Count: Chicago Path. Soc., 1908, vii.

The examination of the chest showed evidence of some pathologic change in the left upper lobe of the lung. Fluid was suspected and a small amount of clear fluid was obtained on aspirating. The patient had very little cough and did not raise enough sputum for examination. No definite diagnosis was made.

Her labor was perfectly normal. We delivered her in the Sims position, as she was more comfortable lying on the left side. The puerperium was normal except for the pain in the chest until the fourteenth day, when she died suddenly shortly after expelling an enema. Her temperature had ranged from 97 to 99 until shortly before death when it reached 100.8. The pulse varied from 102 to 142. The respirations were always a little rapid, ranging from twenty-eight to thirty-eight per minute. There were no complaints of pain or tenderness in the lower abdomen.

A necropsy was performed by Dr. Floyd Riley. The following abstract is taken from his report of Autopsy No. 2133 in the records of the pathologic department of Rush Medical College:

The body is that of a woman 150 cm. long and in fairly good flesh. There is post-mortem discoloration over the back of the trunk and the lower extremities.

On opening the thorax we find the lungs not collapsed. There are marked adhesions between the right lung and the parietal pleura. There is some straw-colored fluid in the right pleural cavity, mostly encysted. The tissues of the anterior mediastinum are edematous. There is much bloody colored fluid in the pericardial cavity. There are marked adhesions between the left lung and the pericardium. The left lung is adherent to the chest wall by extremely dense adhesions which surround a cavity of pus. In removing the lungs from the thoracic cavity a large portion of necrotic left lung is torn away.

On opening the left bronchus, the bronchioles of the left upper lobe are seen to be reddened, while the branches into the left lower lobe appear markedly matted together and their lumina almost completely obliterated by a white tumor mass. The mucosa of these branches is not visible, neither are the normal prominences and depressions, everything being replaced by the irregular projections of the tumor. On section the walls of the branches of the first order appear 2 mm. thick. Those branches of the left bronchus lying toward the periphery of the lung are unchanged. The lung tissue surrounding the branches involved by the tumor is compressed and hard, being also involved by the tumor.

The bronchus of the right lung and its branches are apparently normal.

The tracheal and bronchial lymph-glands are enlarged, black, and contain a white, hard tumor mass.

In the branches of the pulmonary artery are seen masses of thrombi which completely occlude the lumen of the larger branches.

The pericardial cavity contains about a quart of thin bloody fluid. Both layers of the pericardium are covered by a thin layer of not easily removable fibrin. There are no important changes in the heart. The spleen is twice its normal size. There is an accessory spleen the size of a hazel-nut in the omentum. The liver shows signs of a passive hyperemia. By cutting the liver into thin sections two small round tumor nodes, 0.5 cm. in diameter are found in the liver substance. Two gall-stones each 1 cm. in diameter are found in the gall-bladder. A somewhat larger stone is found in the cystic duct. The kidneys are slightly enlarged. In the parenchyma of the kidneys are distributed grayish-white, pin-head sized nodules. The uterus is twice the normal size. In the branches of the uterine veins are to be seen occluding thrombi. The placental site is seen on the anterior wall of the uterus. The tubes and ovaries are free. (The tubes and ovaries were normal.)

A histologic study was made of the left lung, liver, peribronchial lymph-glands, spleen, accessory spleen, pancreas, kidney, adrenals and myocardium.

The sections of the lung, besides showing anthracosis in the region of the thickened pleura, presents tubules of irregular shapes and varying sizes, lined with an uneven, low, deeply-staining, columnar epithelium which in places is more than one layer in thickness. This epithelium does not respect the basement membrane and groups of these cells are scattered thickly throughout the cut sections. This tubulocellular structure has all the microscopic appearances of an adenocarcinoma.

The sections of the peribronchial lymph-gland and liver show tubules and cells of the same nature as found in the lung. These are foci of adenocarcinoma evidently metastatic.

The sections of the spleen, accessory spleen and kidney show on pathologic changes except a marked passive hyperemia. The adrenals show a fatty change throughout the cortex and medulla but are otherwise normal. The myocardium has 2 mm. of fat beneath the epicardium, which at the outer edge is infiltrated with small, round, deeply-staining cells (small round-cells). The muscle fibers show

considerable brown atrophy and between them is more than the normal amount of connective tissue.

Anatomic Diagnosis.—Thrombosis of the uterine veins; puerperal uterus (fourteen days before sudden death); embolism of the pulmonary artery; primary carcinoma of the left bronchus; secondary carcinoma of the trachea and bronchial lymph-glands, pleura, liver and kidneys; chronic adhesive pleuritis with circumscribed empyema; compression atelectasis and edema of left lower lobe; acute fibrino hemorrhagic pericarditis; acute parenchymatous degeneration and passive hyperemia of the liver, kidneys and spleen; cholelithiasis with cystic-duct obstruction; accessory spleen in the great omentum.

April 13, 1914.

REMARKS ACCOMPANYING A DEMONSTRATION OF TWO HEARTS WITH PATENT INTERVENTRICULAR SEPTA, EXTENSIVE SHORTENING OF THE COLON DUE TO ULCERATION (LUES?) AND HUGE CALCULOUS DILATATION OF THE DUCTUS PANCREATICUS WIRSUNGI

Wayne W. Bissell

(From the Pathological Laboratory of Cook County Hospital, Chicago.)

PATENT INTERVENTRICULAR SEPTUM WITH PULMONARY STENOSIS

H. R., an American, 22 years of age, and a farmer by occupation, entered the Cook County Hospital Jan. 23, 1914, to the service of Drs. Miller and Hamburger, complaining of shortness of breath and swelling of the ankles.

History.—Dyspnea had been his chief complaint for the previous three months until about January 1, when he noticed that his ankles and legs were swollen and his abdomen enlarged. He said that he was a "blue baby" but had never suffered any trouble until 10 years old, when he suffered a slight injury in a railway wreck, leaving his heart "weak." Twenty months previous to his entrance in the hospital he

suffered an attack of heart trouble, similar to this present one. There was nothing of note in his family history. He was a heavy drinker, but denied ever having had a venereal infection. Examination revealed a well-nourished young man not acutely ill, but suffering a rather marked dyspnea. His pupils were equal and reacted to light and accommodation. The lips were cyanotic. Moist râles could be heard

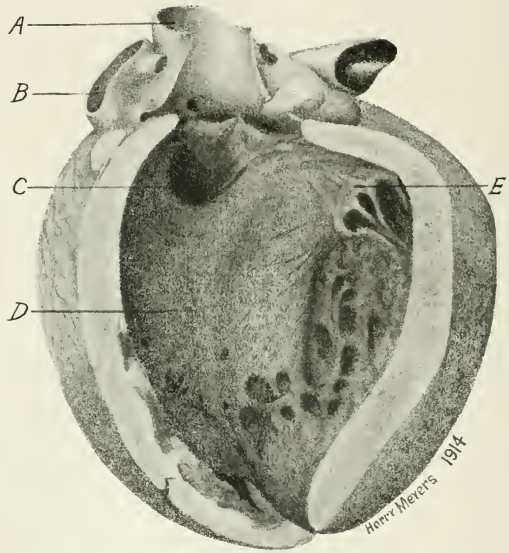

Fig. 1.—Patent interventricular septum with pulmonary stenosis in an adult. A, aorta; B, pulmonary artery; C, defect in the septum; D, left ventricle; E, mitral valve.

plasia of the tracheobronchial lymph-nodes; emaciation; over the entire chest. The area of heart dulness was greatly enlarged; the left border 2 cm. outside the midclavicular line, the right 3 cm. to the right of the right border of the sternum, the upper at the second interspace. A soft systolic murmur was heard at the apex transmitted toward the axilla; there were no murmurs at the base. Rhythm was

regular and the systolic blood-pressure was 128, the diastolic 104.

The abdomen was distended and there were physical signs of a large quantity of free fluid in the peritoneal cavity. There was a marked soft edema of the lower extremities, especially below the knees. The hands were cyanotic and edematous. The average daily output of urine was less than 500 c.c. and a few hyalin casts were found. Nothing abnormal was discovered in the blood. Two days after his entrance

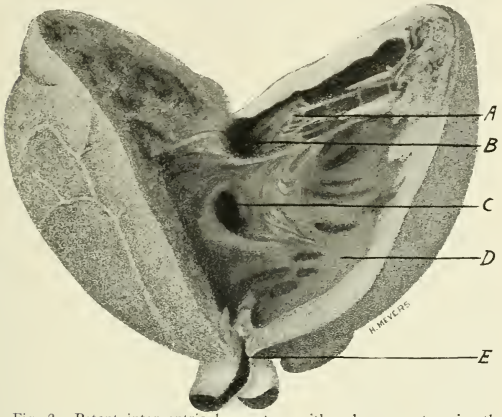

Fig. 2.—Patent interventricular septum with pulmonary stenosis; the opening in the right ventricle and its relation to the tricuspid valve. A, tricuspid valve; B, tricuspid ring; C, defect in the septum; D, right ventricle; E, stenosed and atresic pulmonary artery.

in the hospital 3,000 c.c. of clear straw-colored fluid was removed from the peritoneal cavity and 1,200 c.c. of similar fluid from the left pleural cavity. The temperature remained normal. Two days previous to death the following notation was made on the clinical records:

"Patient has a mitral lesion and general anasarca which has been very persistent. He does not respond well to digitalis or diuretics." Death occurred March 11, 1914.

Anatomic Diagnosis.—Large defect of the septum ventriculare of the heart in the undefended space; marked bulging of the right ventricle opposite this defect; marked congenital stenosis of the pulmonic valve; hypertrophy of the myocar-

dium; extreme dilatation of the heart; thrombosis of the dependent portions of both ventricles and of the auricular appendages; multiple recent infarcts of both lungs; petechial hemorrhages in the skin over the greater part of the body; marked dilatation and engorgement of the vena cava, azogos, internal jugular, the subclavian and innominate veins; atrophic cirrhosis of the liver with marked passive hyperemia and fatty changes; cyanotic induration of the kidneys and spleen; marked hyperemia of the peritoneum; general anasarca; abdominal paracentesis wound; moderate bilateral bronchopneumonia; mucopurulent tracheobronchitis; hyperplasia of the tracheobronchial lymph-nodes; emaciation; general icterus; hypodermic puncture needle wounds of both arms; large persistent Eustachian valve.

A description of the heart is as follows: "This heart (Figs. 1 and 2) is very large. It measures 15 cm. from base to apex and 14 cm. from left to right. The myocardium of the left ventricle measures 18 mm. in the thickest portion of the right ventricle 15 cm. Just beneath the aortic valves there is a defect in the interventricular septum (Figs. 1 and 2, C) that measures 22 mm. in diameter. It is round and on the side of the right ventricle there is a remnant of a valve that is continuous with the tricuspid valve. This valve, however, in no way closes the defect. Opposite this defect there is a marked bulging of the myocardium of the right ventricle. There is a very marked congenital stenosis of the pulmonary valve (Fig. 2, E) with a very slight hypoplasia of the pulmonary artery. The cusps of the pulmonary valve are so fused together that they form a triangular opening which is 7 mm. across in its widest diameter. The ductus arteriosis is entirely obliterated. There is a great deal of coagulated blood in the dependent portions of all the chambers of this heart. The foramen ovale is closed."

TRANSPOSITION OF THE ARTERIAL TRUNKS, PATENT INTERVENTRICULAR SEPTUM AND RUDIMENTARY RIGHT VENTRICLE

Baby G, a white male infant weighing 7 pounds, was born in the Cook County Hospital Feb. 21, 1913, to the service of Dr. Hillis. Nothing abnormal attended his delivery except that he was a "blue baby." He was his mother's third child, the other children being alive and apparently in good health. He was apparently a normal infant, until his tenth day, when a sudden attack of cyanosis led his

physicians to believe that he suffered a congenital cardiac anomaly. Death occurred March 3, 1914.

Anatomic Diagnosis.—Absence of interventricular septum; marked atresia of the right ventricle; absence of direct valvular communication between the atresic right ventricle and the right auricle; anomalous communication between the right and left ventricles; complete transposition of the great arterial trunks; marked dilatation of the common ventricular chambers; passive hyperemia of the kidneys, liver and lung; marked bilateral bronchopneumonia; hyperplasia of the spleen and tracheobronchial lymph-nodes; cloudy swelling of the kidneys.

"This heart (Figs. 3 and 4) is apparently of about normal size; it weighs 50 gm. On opening the heart with an incision just to the left of the usual position of the interventricular septum an absence of interventricular septum is at once evident. There is, however, a band of muscle (Fig. 3, G) pyramidal in shape, with its apex pointing toward the apex of the heart and its base broadening out at the base of the heart, which is apparently a primitive interventricular septum. At the usual site of the undefended space there is a defect (Fig. 3, C) in this primitive septum which leads into a markedly atresic right ventricular chamber (Fig. 4, D). This defect is 8 mm. in diameter and is unguarded as far as any valves are concerned. In its widest dimension this very small right ventricle is 2 cm. in diameter. A large vessel is given off from this chamber which is evidently the aorta, as the coronary arteries (Fig. 4, B) arise from it. The great vessel arising from the left large chamber has no sinuses of Valsalva or coronary arteries. This large chamber, through the near absence of interventricular septum communicates freely with that chamber of the heart which contains a tricuspid valve and on its left a well-formed mitral valve guards its opening into the left auricle. There is no communication between the atresic right ventricle and the right auricle except by way of the left ventricle. The course of blood-stream through this heart must of necessity be from the right auricle to the large common ventricular chamber and to the pulmonary circuit by way of the pulmonary artery, which, as has been said, arises from the left ventricle, or through the defect in the primitive septum into the atresic ventricle and thence out through the systemic circulation."

GREAT SHORTENING OF THE COLON WITH ULCERATION

J. S., colored, 36 years of age, and a janitor by occupation, entered the Cook County Hospital Jan. 17, 1914, to the service of Drs. Kanavel and Wolfer, complaining of acute pain in the abdomen. He had been suffering thus for the past four days. The pain came on suddenly, was very acute, and

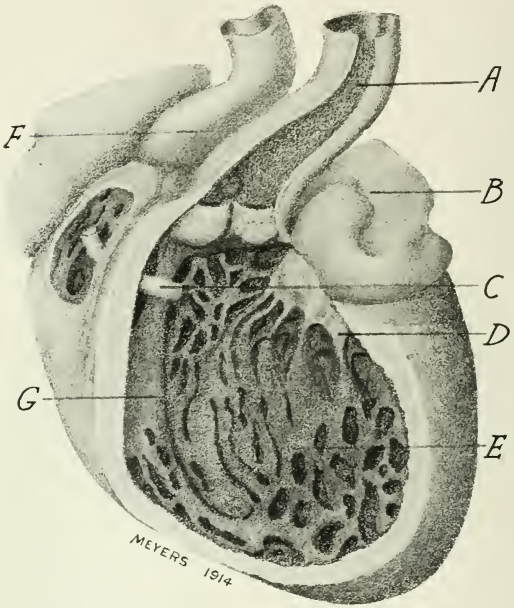

Fig. 3.—Rudimentary right ventricle—almost a cor biatriatum triloculare—with transposition of the large arterial trunks. A, pulmonary artery; B, left ventricle; C, quill passed through a defect in the interventricular septum into the small right ventricle; D, mitral valve; E, left ventricle; F, aorta; G, primitive interventricular septum.

two hours after its onset he vomited. He suffered many chills and in spite of large doses of castor oil and salts, his pain was not relieved, nor was he able to induce a bowel movement.

He had always enjoyed fairly good health with the exception of the diseases of childhood, his only complaint being that for many years he had suffered a chronic constipation. His family history was good, there being no tuberculosis in

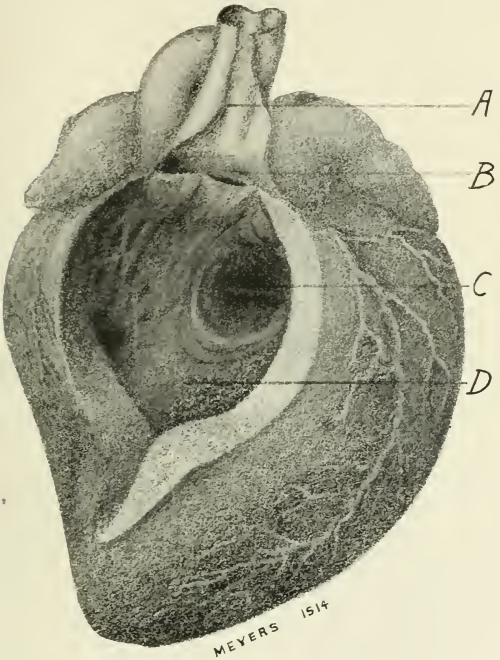

Fig. 4.—Rudimentary right ventricle with transposition of aorta and pulmonary artery. The only entry into this small right ventricle was through the opening C, in the interventricular septum. A, aorta; B, sinuses of Valsalva with coronary artery openings; D, rudimentary right ventricle.

any of his relatives. He was a temperate drinker, and although he volunteered that he had had gonorrhea several times, he denied that he had ever had syphilis.

On examination it is recorded that he was a poorly-nourished and apparently a very sick man. The abdomen was held very rigid. There was exquisite tenderness along the lower border of the liver and in the epigastrium. No tumor mass could be felt anywhere in the abdomen. His blood contained 47,200 leukocytes, of which 87 per cent. were polymorphonuclear neutrophils. Rectal examination revealed nothing abnormal.

An exploratory laparotomy was performed immediately, and it was discovered that the colon was very short and thick and that in the region of the hepatic flexure there was a perforation with a localized fibrinopurulent peritonitis. The condition of the patient was so poor that this perforation was not dealt with, but rapid closure with drainage was made. He died Jan. 19, 1914, within twenty-four hours after operation.

Anatomic Diagnosis.—Healed fibrous and chronic ulcerative colitis; multiple suppurative diverticulitis with perforation of the colon at the hepatic flexure; acute generalized fibrinopurulent peritonitis; recent repaired laparotomy wound; three large drainage tubes extending to the under surface of the liver; hypodermic puncture needle wounds of both arms; hyperplasia of the spleen; cloudy swelling of the liver, spleen and myocardium; syphilitic aortitis; emaciation; missing and gold-crowned teeth.

"This colon is very short and thick and it is surrounded by a layer of fat averaging 3 cm. in thickness (Fig. 5). It measures 44 cm. in length from the ileocecal junction to the anal margin. The mucous membrane, especially of the transverse and descending portion, is thrown into longitudinal folds, which have the appearance and texture of dense, fibrous scar tissue. Between these folds there are many minute diverticula (Fig. 5, D and E) which will admit the blunt end of an autopsy needle and contain a sanguinopurulent exudate. At the hepatic flexure of this colon there is an ulcer 2 cm. in diameter and of irregular outline, in the center of which is a perforation 1 cm. in diameter opening into the free peritoneal cavity (Fig. 5, C). The wall of the cecum and ascending colon is greatly thickened, but its lining is much smoother and its lumen less constricted than that of the descending colon. From the seat of perforation to the rectum the constriction becomes gradually tighter until at the level of the internal sphincter the constriction is so tight that it scarcely admits my little finger."

Microscopic preparations taken from many places throughout the length of this colon were examined and the changes

are those of a chronic inflammation resembling syphilis in some respects.

HUGE CALCULOUS IMPACTION OF THE PANCREATIC DUCT

C. A., Swedish, 49 years old, entered the Cook County Hospital Jan. 26, 1914, to the service of Dr. Lewison. He was greatly emaciated and very weak. He had been well up to eleven months previous, except for an attack of "obstruction of the bowels" in his thirty-sixth year, for

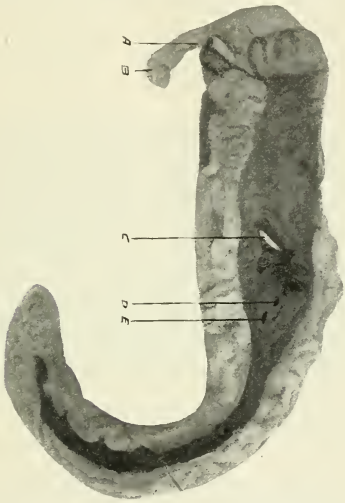

Fig. 5.—Great shortening of the colon with (syphilitic?) ulceration and perforation. A, ileum; B, appendix; C, perforation at the hepatic flexure; D and E, diverticula.

which he was operated. For nearly a year he had been growing weaker and thinner in spite of an unusual appetite, and he noticed that he was passing more urine than usual. Three months previous to his admission he began to cough some, but he never expectorated very much and had no night sweats. He had lost 35 pounds in weight. A sister, with whom he had lived, died of pulmonary tuberculosis.

When he entered the hospital there were physical signs of consolidation and some cavity formation of the entire right lung and the apex of the left lower lobe. There was a post-operative ventral hernia in the left lower quadrant of the abdomen. Tubercle bacilli were found in the sputum. Sugar was present in the urine. Throughout his stay in the hospital there was a slight evening rise of temperature. He grew progressively weaker and death occurred Feb. 10, 1914.

Anatomic Diagnosis.—Multiple concretions and marked dilatation of the pancreatic duct; marked atrophy of the pancreas; healing furuncle of the nape of the neck; bilateral caseous and ulcerative pulmonary tuberculosis; acute tuberculous bronchopneumonia; nodular caseous tuberculosis of the kidneys and spleen; hyperplasia of the tracheobronchial and mesenteric lymph-nodes; serofibrinous pericarditis;

Fig. 6.—Photograph of a gelatine cast of the dilated duct after removal of the calculus. This cast is 13.5 cm. long, 2 cm. in its greatest diameter and at A the widening in the ampulla occurs.

right serofibrinous pleuritis; left obliterative fibrous pleuritis; catarrhal tracheobronchitis; cloudy swelling of the kidneys and liver; extreme anemia and emaciation; abnormally long, redundant colon; atrophic laparotomy scar; absence of the distal phalanges of the first and second toes of the right foot.

A description of the pancreas is as follows: "It is 16 cm. long, 2.5 cm. in thickness at the head and 1 cm. in thickness at the tail. The pancreatic duct (Fig. 6) is markedly dilated and filled with clear, watery fluid. There are numerous concretions within the lumen, fixed in position by delicate fibrous strands and septa. The opening of the duct into

the ampula of Vater is completely occluded by a well-molded concretion (Fig. 6, A). There is apparently complete atrophy of the glandular tissue."

Microscopic preparations taken from many places about this huge pancreatic duct contain tuberculous granulation tissue, but in no place was I able to find any pancreatic tissue.

In a brief search of the literature I am unable to find reports of similar huge dilatation of the ductus pancreatus Wirsungi.

TRANSACTIONS OF THE CHICAGO PATHOLOGICAL SOCIETY

VOL. IX. DECEMBER 1, 1914. NO. 5.

PRESIDENTIAL ADDRESS

ERNEST E. IRONS

Shortly after the death of Professor von Neusser, one of my colleagues, in discussing his ability as a clinical teacher, remarked how great the misfortune to medicine that experience is not hereditary. A moment's consideration, of course, presents drawbacks which undoubtedly would more than compensate for the advantages of such an arrangement, but nevertheless one cannot but pause to imagine the results to medicine if the experience and acumen of the masters might be transmitted to their sons. Much of the art of medicine and many of its traditions are handed down from master to pupil by personal contact and example, and together with information, largely that of pathology and clinical observation, preserved in medical writings constitute the heritage of each generation of physicians. We all derive inspiration from reading the clinical lectures of such masters as Trousseau or Sydenham, but even in these classical writings we can see how the more recently developed facts of the framework of medicine, pathology, are necessary to fill the gaps in clinical observation, now changing shrewd speculation into established fact, now necessitating complete reconstruction of the conception of the process of disease. The whole structure of clinical medicine is undergoing a continual rearrangement, and pathology is seen to be not a dead but a very live science, which rightfully demands of all other branches of medicine continual recognition and consultation. It is worth remembering, too, that the ultimate object of pathology, as of physiology, anatomy and allied sciences, is not merely the acquire-

ment of knowledge, but of knowledge which in its application shall aid in understanding the causes, prophylaxis, course and cure of disease, to the end that human suffering may be diminished, the span of service to fellowmen prolonged and the total of human happiness increased.

The growing complexity of modern medicine has necessitated an increasing division of labor, so that the anatomist, physiologist, pathologist and serologist has each developed his own special branch, carrying his researches far beyond the bounds possible without this specialism. This division of labor has been of enormous value to medicine, but it is exerting also an unfavorable influence on medicine of the present day. The intense study of one subject, while necessary and in itself advisable, easily leads to neglect of allied sciences, and with the loss of the perspective of medicine as a whole the interpretation of observed facts becomes fallacious. Conan Doyle expresses this thought as applied to other fields of research: "Breadth of view is one of the essentials of our profession. The interplay of ideas and the oblique uses of knowledge are often of extraordinary interest."

The laborers in specialized groups are hewing the stones for the edifice of medicine, often at the expense of infinite labor and time. As the construction progresses, many blocks fall readily into place. Occasionally stones prepared long ago and laid aside are brought to light to take their places in the building, so that we have been taught to believe that all stones possess a potential value which may become evident as the structure rises. No doubt some day we shall employ some of these unused and strangely fashioned stones, but we cannot but wonder whether the mass of unutilized material might not be prevented from further undue increase by a closer acquaintance of the workers with the general plans of the building. Isolation of the worker limits the value of his output and he expends prodigious labor with the sole idea of shaping stones, without regard to whether there is any chance of their being available for use in the edifice. As a corrective of this undesirable isolation, the Chi-

cago Pathological Society offers its members one very efficient means for the interchange and broadening of ideas and the conservation of effort.

Perhaps the most unfortunate and least justifiable of the lines of cleavage in medical endeavor is that which assumes sharply to divide the activities of the pathologist from those of the clinician, and at the door of the latter lies most of the responsibility for this widening breach. It is true that the immediate interests of the clinician are found among the living, those of the pathologist among the dead, but these interests are most intimately related—the work of one complements and is only possible through that of the other. The clinician to be truly successful must be a pathologist, and construct his conception of the ailment of his patient from symptoms and signs interpreted in the light of a wide post-mortem experience, just as the able pathologist is a clinician, and can reconstruct the essentials of the picture of the fatal illness from the pathologic conditions he finds at necropsy. To us of the younger generation of medical men, this necessity of keeping close to gross and microscopic pathology requires greater emphasis now than ever before, particularly in view of the growth of the newer fields of serology and chemicophysiology, the study of which while necessary to our growth in medicine, offers at the same time an additional distraction from the older fundamental branches, with which our elders did not have to contend.

The neglect of the post-mortem has well been termed the weakest point in American medicine. Popular prejudice, aided by unfortunate laws, is responsible in a large part for our delinquency in the control of clinical observation by post-mortem examination, but neither these hindrances nor a year spent at the necropsy tables of Europe furnish adequate excuse for the neglect of the post-mortem by our younger men. When diligent effort is made, even under the present unfavorable legal conditions, the percentage of post-mortems rapidly increases, and it may not be out of place to remark that the best stimulus for such diligent effort is a carefully kept and complete history sheet.

To the past services of pathology to medicine, no tribute is necessary. It has furnished the basis as well of our therapeusis, as of our physical diagnosis and at the same time has been a restraining hand, curbing fanciful diagnosis, warding off from the empiric and inclining toward the rational. Many of the therapeutic mistakes and most of the absurdities of modern medicine could be avoided by due regard to what is already known and well established regarding the pathology of disease.

Pathology serves the individual as well as the collective profession. The lessons of mistakes revealed at the post-mortem table are fixed in the memory as are no others. The explanation of obscure apparently unrelated nervous symptoms by the demonstration of multiple fibromata of the central nervous system, the finding of coronary obstruction and myomalacia in the subject of unusual or prolonged cardiac disturbance, or the presence of a neoplasm in the chest which accounts for profound circulatory disturbances and confusing physical signs afford keen satisfaction to the enthusiastic student of disease. The multitude of facts and the endless combinations of syndromes which must be remembered in the practice of medicine are most readily available for use if kept in the pigeon holes of pathologic classification.

But the services of pathology to medicine are not confined to the past. It is taking a very active part in the development of medicine of the present and promises further material assistance in the solution of medical problems. How many deaths reported as uremic are really due to cerebral hemorrhage, meningitis, brain abscess or basal skull fracture? Even when the history and physical signs seemed to indicate the diagnosis with a fair degree of certainty, the post-mortem shows that we were entirely wrong. Adequate statistics which shall inform the clinician of what he may expect and thus give him the benefit of the knowledge of probabilities under given conditions can only be furnished by the pathologist with the cooperation of his colleague.

The solution of the problem of cancer is dependent to a very large extent on the pathologist. The brilliant and painstaking researches of one of our members reported last year in this society in the course of which the hereditary incidence of spontaneous tumors in mice was traced for many generations, corresponding to centuries on centuries of human life, present facts which will have an important influence on future studies of cancer in man.

Veterinary pathology offers much valuable information, particularly in the proving of methods devised for the artificial establishment of immunity to disease, and we welcome to the society those who are specially interested in this department of pathology in which the facilities for the experimental demonstration of therapeutic methods so far exceed in many respects those of human medicine.

The data and methods of serology and immunity differ for the most part from those of cellular pathology, but even these newer departments of medicine owe much to the assistance rendered by gross and microscopic pathology. Our knowledge of serum disease and allergy has been greatly advanced by studies on the pathology of anaphylactic shock. A slight change in the conception of the pathology of epidemic meningitis, modified the method of use of antimeningococcic serum, so that a remedy which was of but doubtful value when given subcutaneously or intravenously became at once a definite savior of life when introduced into the subdural space.

The value of antitetanic serum in the prophylaxis of tetanus has long been conceded, but as a curative agent in the developed disease, antitoxin as generally used by subcutaneous injection has failed to reduce the mortality more than about 20 per cent. below that of cases treated symptomatically. Within the year combined pathologic and serologic studies have proved that tetanus toxin traveling centralward along peripheral nerves is not, as has usually been held, beyond the reach of antitoxin, but can be reached and successfully combated by intraspinal injection. This method combined with intravenous injection promises to

reduce a previous mortality of serum treated cases from 60 per cent. to from 30 to 40 per cent.

These are only a few familiar instances of the advances attainable through the cooperation of the collateral branches of medicine with gross and microscopic pathology. New ideas and improved methods will come, as they have in the past, not from the worker who strives to increase his isolation, but from him who while pushing forward in his own specialty at the same time maintains a broad and intimate acquaintance with progress in other lines.

From a small group of men meeting in 1878 to observe and discuss interesting specimens, the Chicago Pathological Society has grown to a membership of 173. The special interests of our members, while still essentially those of pathology, have become diversified with the growth of more special lines of pathologic research, and problems in bacteriology, physiology, anatomy, chemical pathology and immunity share our evenings with the older subjects of gross and microscopic pathology. By this broadening of scope the society has kept pace with the increasing complexity of medical knowledge, and each of us is afforded an opportunity of learning at first hand of the advances beyond the limits of his own particular line of endeavor. The diversity of subjects offered for discussion in our meetings testifies to the multiplicity of interests which can be successfully united in a society whose object is the demonstration of scientific truths, whose criticism is tempered with kindness, and within whose membership there is no taint of unhealthy personal rivalry.

The growth of the society has brought with it none of the disadvantages of diffuseness, for each of us has an active interest in all branches of medicine represented. Further natural expansion is to be encouraged. Beside affording opportunity for mutual benefit by the interchange of ideas of its members, this society presents in its Transactions a medium for the publication of original researches. We are now in a position to assure prompt publication of papers, provided they are handed to the Secretary as soon as presented.

Failure to furnish copy on time has occasioned most of the past delay in publication. A few hints as to the desirability of brevity and the omission of needless detail, long citations from the literature and tedious descriptions, given by those of us who have oversight of the work presented by younger members at their first appearance before the society, will remove much of the embarrassment of the speakers and add to the profit of their auditors.

A long-felt need of the society is that of a permanent home. The present hall is inadequate, but it has seemed wise to continue our meetings here for this year. We shall look forward to the time when we can have a permanent and properly equipped meeting place. Meanwhile the lack of ideal quarters need not interfere with our work.

May the meetings of this coming year increase in value and interest and we ourselves bear in mind the importance of corelation and cooperation among our several lines of endeavor, and particularly the importance of keeping close to pathology.

Oct. 12, 1914.

AN ACID-FAST STREPTOTHRIX (NOCARDIA)

DAVID J. DAVIS

(From the Department of Pathology University of Illinois, Chicago.)

There is a fairly well-defined group of infections, the great majority of which are pulmonary, caused by weakly acid-fast, branching, mycelial growths which do not form ray-like granules. These cases clinically are not distinguished ordinarily from tuberculosis. A case is here cited in which the pulmonary lesions were very probably caused by such an organism.

A man 64 years of age had been troubled for a long time, probably several years, with chronic cough. He then suddenly developed symptoms of pleurisy and bronchopneumonia. At this time the cough and expectoration were increased markedly. The sputum

was green and highly purulent. In smears were seen many acid-fast, Gram positive, mycelial clusters along with many cocci and bacilli. These mycelial growths were found most abundant in the thick green masses of sputum. They appeared constantly for several weeks, then gradually disappeared as the general symptoms abated.

Potassium iodid was given which might have had some influence on the course of the disease. The patient recovered sufficiently to go to work and at present is practically well except for a slight cough. There is little expectoration and no acid-fast organisms are now in the sputum.

Roentgen-ray examination of the chest suggested tuberculosis. No tubercle bacilli could be found. Guinea-pig inoculations with large amounts of sputum gave negative results.

Numerous attempts to grow the acid-fast organism under various conditions failed. It is both acid and alcohol fast. Strong acids, however, decolorize it more easily than they do tubercle bacilli. It does not resist antiformin.

This organism evidently belongs to the group of acid-fast streptothrices. It is what Homer Wright would call nocardia.

Jan. 12, 1914.

TREATMENT OF GONORRHEA AND ITS COMPLICATIONS BY ANTIGONOCOCCIC SERUM*

B. C. CORBUS, M.D.

CONCLUSIONS

1. The complement-fixation test is a reliable guide in the administration of the serum. When the test is negative, the serum should not be used.

2. The intensity of the positive complement-fixation test offers a reliable guide as to whether or

* The complete paper will be found in the Jour. Am. Med. Assn., 1914, lxii, 1462.

not the serum will be efficient, as the efficiency and intensity are in direct proportion.

3. The amount injected should be at least from 36 to 45 c.c., administered intramuscularly, from 12 to 15 c.c. a day, for three days.

4. Serum-sickness, if distressing, should not be alarming.

5. A negative complement-fixation test after two or three months shows a complete cure.

March 9, 1914.

THE PRIMARY SPONTANEOUS TUMORS OF THE LUNGS IN MICE*

MAUD SLYE,
HARRIET F. HOLMES
AND
H. GIDEON WELLS, M.D.

(From the Otho S. A. Sprague Memorial Institute and the Pathological Laboratory of the University of Chicago.)

SUMMARY

In a pedigreed stock of mice, bred with special reference to the study of the influence of heredity on the incidence of cancer, and as far as possible allowed to live out their full lives and die a natural death, there were found 160 mice with primary lung tumors in 6,000 necropsies, about 4,000 of which were in mice of 1 year of age or over. Such tumors rarely appear before the mice are 1 year of age, so the incidence in the mice of tumor age was 4 per cent. They seem to arise from areas of lung tissue in which inflammatory hyperplasia has occurred, and may originate from either the alveolar or bronchial epithelium; usually they are subpleural, and the majority seem to arise in the alveoli. A complete series is found from inflammatory hyperplasia through benign papillary overgrowths to typical papillary adenocarcinomas with extensive metastases. In the 160 cases here described there were four with metastases into mediastinal

* The complete article will be published in the Jour. Med. Research.

glands, including one with secondary growths in the diaphragm, thoracic wall and kidney, and one with metastases in the chest wall, these being the first recorded instances of metastases outside the lungs resulting from primary lung tumors in mice. Of the others, sixteen showed metastases throughout the lungs, and forty-three were infiltrating and of definitely malignant character, a total of sixty-three malignant and ninety-seven benign growths. Mitotic figures are rare; amitotic division common. Metastasis takes place most often through the air passages, but also through blood-vessels and lymphatics, tumor thrombi having been found in both. Of 155 cases studied with reference to ancestry, 146 occurred in mice with a cancer ancestry, and this included all the typically malignant tumors; the metastasizing tumors occurred in strains that were of highly cancerous ancestry. The nine tumors found in mice of non-cancer ancestry included only one with some evidence of possible malignancy, the other eight being simple benign papillary adenomas or early growths that could be distinguished from inflammatory hyperplasia only with difficulty. Apparently mice with cancer heredity react to non-specific inflammatory conditions more often with excessive proliferation which leads to malignancy, than mice of non-cancerous ancestry.

We have not found any striking relation between nematodes and lung tumors. In frequency the lung tumors in this stock rank next to the mammary gland tumors, constituting about one-third of all spontaneous tumors. In the 160 mice with lung tumors, fifteen had more than one such primary growth, and twenty-three had one or more primary neoplasms in other organs. There were 42.6 per cent. of males and 57.4 per cent. of females in this series.

A common symptom in mice with lung tumors is an inflammatory swelling about the eyes, leading to destruction of the eye from scratching; this may aid in diagnosing lung tumors during life, and permit of securing for breeding experiments male ancestors with tumors.

May 11, 1914.

A CASE OF CONGENITAL MEGACOLON (HIRSCHSPRUNG'S DISEASE)

V. H. MOON

The case here described occurred in the Hospital of St. Anthony de Padua, Chicago, in January, 1914. It is through the courtesy of Dr. Cupler, to whom the child was brought, and of Dr. Heusinkveldt, of the resident staff, that the case is here presented. On the following findings and history the diagnosis of the disease was made:

The patient, a boy aged 4 years, entered the hospital with a markedly distended abdomen, which condition was noticed soon after birth and had steadily grown more pronounced. The child had always been weakly and difficult to nourish, and would sometimes go several days without a bowel movement unless resort was made to artificial means. The head, neck and limbs were emaciated and presented a marked contrast to the greatly distended abdomen. The ribs were prominent, the costochondral junctions were beaded and the costal margins were much expanded and everted. Râles were heard over the upper part of the chest. The heart sounds were normal. The abdomen was tense and tympanitic. The rectum presented no stenosis or hindrance to the introduction of a finger or catheter. At this time there was no constipation, the child having four or five stools daily of a greenish color and containing mucus. A quantity of a suspension of bismuth subnitrate was introduced per rectum, following which a skiagraph of the abdomen was made. This showed the distended sigmoid occupying the pelvis and lower abdomen in the midline. Diagnosis was made of congenital dilatation of the colon, and operation was decided on. Before the operation could be performed the child developed a bronchial pneumonia and died. A partial necropsy was performed with the following findings:

The abdomen was distended by a greatly enlarged colon. The stomach, liver and diaphragm were displaced upward. The lungs were much compressed and showed regions of consolidation. The colon was removed for further examination. It measures 83 cm. in length along the mesenteric attachment, and 97 cm. along the margin opposite the mesenteric attachment. Its circumference at the ileocecal junction is 14 cm., gradually increasing to a maximum of 36 cm. in the descending colon, from which point it rapidly diminishes to about normal in the upper portion of the rectum. There are no

fibrous bands, folds nor constrictions present which would seem to cause mechanical obstruction of the bowel at any point. The walls of the colon vary from 2 mm. to 4 mm. in thickness with an average of 3 mm. The increased thickness is due to a medium degree of hyperplasia of the musculature, together with a slight increase of the fibrous elements of the submucosa and outer coat. There is a well-marked condition of chronic colitis evidenced by necrosis and desquamation of the epithelium of the bowel, together with a medium grade of round-cell infiltration. Along the margin of the mesenteric attachment there are about 200 lymph nodules, varying in size from 0.3 cm. to 1 cm. in greatest diameter. The transverse bands of the colon are much less conspicuous than normally. The appendix is free and measures 8 cm. in length and 0.7 cm. in average diameter.

The condition of hypertrophy and dilatation of the colon has been variously characterized as congenital megacolon, congenital idiopathic dilatation of the colon, giant colon, or Hirschsprung's disease. A case of great dilatation of the colon was reported by Parry in 1825. A number of cases were reported between that time and 1888 when Hirschsprung[1] in a study of the condition brought forward evidence of its congenital origin. The first case reported from America was by Lewitt,[2] then a demonstrator of anatomy in Rush Medical College. His report was similar to previous ones in that the congenital origin of the condition was not suggested.

Congenital megacolon manifests itself usually during the first year of the child's life. Its symptoms vary from a sluggish condition of the bowel with infrequent movements to a complete stasis or obstipation with great distention of the abdomen. Often exaggerated peristaltic waves can be seen through the thinned-out abdominal wall. Nutritional disturbances, anemia and emaciation are described as characteristic sequences. The costal margins are expanded and everted by the distention of the abdominal contents, the diaphragm being driven upward and the thoracic viscera compressed. Unless treated surgically the condition usually terminates in death, which may be

1. Jahrb. f. Kinderh., 1888, xxvi.
2. Chicago Med. Jour., 1867, xxiii, 359.

preceded by colitis, ulceration of the colon, perforation and peritonitis, or it may be from an intercurrent infection to which the child's weakened condition predisposes. Occasionally cases live through childhood to adult life. Fourmad[3] reports a case in which the patient lived to the age of 29. The man had shown typical symptoms since early infancy, with increasing distention of the abdomen. He was exhibited in a dime museum as the "human wind-bag" or the "baloon man." The cause of death was not stated. At necropsy the body length was 5 feet 7.5 inches, while the circumference of the abdomen was 7 feet 2.5 inches. The colon in this case was 252 cm. in length, 76 cm. in greatest circumference and contained about 40 pounds of fecal material. Dilatation as extreme as this is rare, but all grades exist from this extreme to those in which the dilatation is barely noticeable.

The essential pathology of congenital megacolon is simple, consisting in the main of dilatation of part or all of the large bowel, accompanied usually by varying grades of hyperplasia of the muscular coats. Lowenstein[4] in reviewing the pathology of 83 cases found that it involved the sigmoid alone in 27 cases; more than one portion of the colon but not the entire colon in 35 cases; the entire colon in 11 cases; the colon and rectum in 6 cases, and some part of the small bowel as well as the colon in 4 cases.

A satisfactory summary of the features of the reported cases is impracticable, for the reason that many cases are reported in adult life or old age without history of trouble beginning in infancy. Thus the observers have failed to differentiate between the true congenital megacolon and the pseudomegacolon occurring as a result of chronic constipation or mechanical obstruction in adult life, and have not recorded sufficient data regarding the cases to make such a distinction possible. Lord Barrington[5] publishes a very complete and satisfactory record of nineteen cases occurring in the London Hospital in children under 12 years of age. This report, together with that of

3. Tr. Col. Phys., 3s, 1892, xiv, 115.
4. Centralbl. f. allg. Path., 1907, xviii, 929.
5. Brit. Jour. Surg., 1914, i, 345.

Lowenstein mentioned above and Finney,[6] so completely covers the field that an attempt at an exhaustive review of the subject would be merely a repetition of work done by others.

The theories advanced as to the origin of megacolon may be briefly summarized as follows:

1. Anatomic or mechanical malformation, as congenital elongation of the bowel with loop formation and resulting obstruction; abnormally long mesentery permitting torsion and obstruction; fibrous bands hindering the free passage of the bowel contents, etc. That such factors are sufficient to cause dilatation of the bowel when present is conceded, but many cases come to operation or to necropsy in which no evidence of mechanical obstruction can be demonstrated.

2. The presence of a neuropathic condition. This conception is based on the theory that faulty or imperfect innervation of the muscular coats of the bowel would cause dilatation of that segment and the resulting stasis would lead to functional hypertrophy of the musculature above the paralyzed segment. However, histologic studies of the bowel walls have been made in many cases and have failed to demonstrate any abnormality in the nerve plexuses which supply stimulation to the bowel muscles. The powerful peristaltic waves so frequently observed would speak against either a faulty innervation or an aplastic condition of the musculature.

3. Inflammation. Some observers claim that the dilatation is due to a colitis becoming chronic. Great distention results from altered chemical conditions in the feces with enormous production of gas. This makes peristalsis difficult, causes dilatation, and finally results in hypertrophy of the muscular coats. Other observers, however, urge that when colitis is present with megacolon it is usually a late manifestation of the condition, and is to be explained as a result rather than as a cause of the dilatation.

4. Valve action at the rectum. Some observers have shown that while the rectum may be perfectly patent apparently, and will admit the passage of a

6. Surg. Gyn. and Obst., 1908, vi, 624.

tube, or the injection of fluids from below, it exerts a valve-like action and completely obstructs the passage of fluid or fecal material from above. This was demonstrated by injecting water through a previously established artificial anus. The water distended the bowel and would not pass out through the rectum. This is accepted by many as the explanation of many cases, but Perthes who made this demonstration admits that it will not explain all cases.

5. Congenital dilatation. This theory is that the dilatation and hypertrophy are in themselves congenital conditions and are present at birth. This view, advanced by Hirschsprung has been substantiated many times by the finding of well-marked dilatation and hypertrophy of the colon present at necropsy on very young infants.

It must be said, however, that each of the above theories is probably the correct explanation in certain cases, and that no one theory will explain every case.

One interesting feature for which no satisfactory explanation has been advanced is the marked predominance of males among the cases of true congenital megacolon. In Barrington's series of 19 cases, 16, or 84.2 per cent., were males. A similar proportion holds among the reports of others.

May 11, 1914.

A DISEASE IN GUINEA-PIGS RESEMBLING SCURVY CAUSED BY FEEDING MILK

J. J. MOORE AND D. J. DAVIS

(From the Department of Experimental Medicine, University of Illinois, Chicago.)

A year ago a peculiar affection was noticed in a number of guinea-pigs in the laboratory of St. Luke's Hospital. When moving about the cage they appeared partly paralyzed, dragging their legs and walking with difficulty. The muscles of the legs and the tissues especially around the knee-joints and the wrist-joints were swollen. The animals showed some emaciation. An epidemic disease of some kind was suspected.

Upon investigation we found that the diet of the affected pigs, in addition to oats, green vegetables, hay and water, consisted largely of milk from a cow having experimental streptococcal mastitis. We at once became suspicious of this milk diet, as there was no such disease before it was used. Experiments were designed to ascertain what factors in the diet were responsible.

Different groups of animals were fed on (1) plain milk, (2) milk to which there had been added broth cultures of streptococci, (3) milk boiled for from fifteen to thirty minutes, and (4) streptococcus broth. The animals in Groups 1, 2 and 3 all consumed the milk readily and gained rapidly in weight for a period of from two to three weeks. At the end of this time the weight increase suddenly ceased and simultaneously symptoms like those observed in the first animals appeared.

These symptoms in brief are as follows: Usually the wrist-joints become painful on pressure followed by palpable swelling in the course of from twenty-four to forty-eight hours. The joints continue to increase in size until they are two to three times as large as normal. In some instances after two or three days the knee-joints undergo similar changes, while occasionally the ankle, elbow and shoulder-joints become affected in the order named. The calves of the hind legs are frequently swollen and the skin over the affected muscles may turn blue (seen especially in white pigs), and undergo the changes commonly observed following bruises. At first the swollen parts are soft, but as they gradually decrease in size they become firmer and after two to four weeks the enlargements are chiefly confined to the ends of the long bones which become deformed and hard in consistency. Fractures of the long bones near the epiphyseal junctions are common, the healing of which might result in further deformity. Exostoses are frequent, especially if the milk diet is continued from four to five weeks.

The group of animals fed with streptococcus broth became very much emaciated, but none was afflicted with the disease. Cultures made from the blood, joints and cavities of the guinea-pigs receiving the milk diet and dying of the disease gave, as a rule, negative results. Inoculation of a healthy animal with the blood of a diseased animal did not transmit the disease. Experimentally there is no reason to think that the condition is infectious.

We have repeated the experiments several times, and have always produced the lesions in young pigs, weighing from 100 to 150 grams. Older animals have the lesions less frequently. It is to be noted that raw milk produces the disease as promptly as boiled milk.

Guinea-pigs fed on milk and oats also developed symptoms, as did three of six guinea-pigs fed on milk, oats and green vegetables. Similar lesions were produced in two pigs fed on pure casein in water, but animals fed on lactose water gave negative results.

We have produced a similar condition in guinea-pigs with a diet of oats and water and with a diet of bread and water. It may be questioned whether or not this is the same disease as that caused by feeding milk. While in a general way it is very similar, it was noted that hemorrhages were more frequent and more extensive, and that looseness of the molars was more often observed. Fractures of the long bones also seemed to be more common.

The chief gross pathologic lesions noted post mortem are intramuscular and subcutaneous hemorrhages usually near the joints; enlargements of the ends of the long bones, especially the lower end of the radius and ulna; enlargements of the costochondral junctions, and edema of the subcutaneous tissues. The enlargements of the bones are often accompanied by fractures near the epiphyseal junctions. Hemorrhages are found in very few instances within the joint cavity. The joint surfaces are usually smooth, the changes occurring in the epiphyseal region and periarticular structures. In one animal submucous hemor-

rhage was seen at the base of the lower incisors; looseness of the molars appeared in two other animals. In general, the viscera revealed no important gross lesions.

A number of articles in the literature bear on this subject. Bolle years ago apparently was the first to call attention to a condition in guinea-pigs produced by feeding milk and noted its similarity to scurvy. In 1905 Bartenstein further studied this disease. In 1907 Holst and Frölich made an extensive study of a similar condition in guinea-pigs produced by feeding grains and bread. They also were able to cause lesions by feeding milk, but contended that these lesions were different from those caused by feeding grains. They noted that a general diet containing vegetables would cure the disease. The lesions consisted of hemorrhages, especially about the extremities and about the bones, fractures of bones, hyperemia of gums and looseness of teeth. A few other reports appear in the literature, especially in that on scurvy and rickets.

The following points are noted in conclusion: The young guinea-pig is highly sensitive to slight alterations in diet. A one-sided diet of milk (raw or boiled), grains, bread, etc., will cause lesions chiefly hemorrhagic in character and which involve especially the osseous system, giving rise to bony deformities and pathologic fractures. The more or less acute changes may be checked by giving a general diet but the bony changes, to a considerable degree at least, persist for a long time. The late manifestations require further study.

If we attempt to find the analogue of this disease in the human we would say that it resembles infantile scurvy more closely than any other disease. There are points of resemblance, however, to rickets, multiple exostoses and ecchondroses, osteomalacia, fragilitas ossium, the purpuras and anaphylactic intoxications. The observations reported in this paper may furnish an experimental basis for the study of several obscure diseases of the osseous system.

May 11, 1914.

THE HISTOLOGIC CHANGES IN THE BONES AND JOINTS IN A DISEASE OF GUINEA-PIGS RESEMBLING SCURVY AND CAUSED BY FEEDING MILK

LEILA JACKSON AND E. R. LECOUNT

(From the Pathological Laboratory of St. Luke's Hospital, Chicago.)

We have examined sections from the joints of eleven guinea-pigs, and after determining in a general way the nature of the changes, we arranged them in order as regards the early and latest changes. This was found to correspond closely with the periods on the protocols subsequently furnished us by Drs. Moore and Davis. The duration of changes in all of the eleven animals is not known exactly, therefore the comparison could only be imperfectly carried out.

Because considerable support for the explanation we have to offer of the changes is derived from this correspondence between the stage of the process and the duration, the following tables are given. The tissues consist principally of joints and were from guinea-pigs numbered I. II, III, VII, XI, XII, XV, XVI, XVIII, XXII, XXXII; the sections were grouped according to the changes as follows:

TABLE 1

Changes	Guinea-Pigs
Acute changes hemorrhages and necroses....	I, II, XII, VII, XVI
Subacute changes, osteoid and partly cartilagenous calluses	VII, XXXII, XVIII, III
Cartilagenous calluses.....	III, XXII, XV, XI
Bony calluses	XVI, XI

The period of experimentation was learned regarding only six of the animals and is as follows:

TABLE 2

Number of days after feeding was started	15	21	35	51	68	69
Acute changes hemorrhages and necroses	..	..	..	XVI	..	..
Subacute changes, osteoid and partly cartilagenous calluses XXXII		XVIII	..	..	..	..
Cartilagenous calluses.....	..	..	XXII	..	XI	XV
Bony calluses	..	..	..	XVI	..	XI

Aside from the general accord between the arrangement of the sections and the intervals, so far as known,

of the duration the animals were under experimentation, there is a matter of great moment in the observation of acute changes in the sections studied from Animal XVI, together with very chronic changes, "bony calluses," and the bearing of this will be pointed out presently. At first glance in Table 2, this constitutes an exception difficult to explain.

The changes possess two characteristics: (1) they are apparently not an inflammation but a repair, and (2) they have followed in practically all instances, so far as we can judge, an injury of considerable intensity and suddenness in part at least accompanied by hemorrhage, an injury inflicted but once. There is a necrosis close to the epiphyseal cartilage of the long bones and always on the side of the diaphysis, a sharply outlined necrosis affecting the bone marrow chiefly, the cartilage slightly and as a rule greater about the margins of the shaft than in the center. Sections of the ribs from Animals II, III, XI, XV, XVI and XXII, of the knee-joints from I, VII, XII and XVIII and of the wrist-joints from VII, XVI XXII and XXXII were studied.

The changes after this necrosis, which as previously stated, is in many instances accompanied by hemorrhages, are in all essentials similar to those following the repair of a fracture; in fact, some degree of fracturing is present about many of the cartilages, but rarely on both sides in any one section. As the result of healing, small rounded masses of cartilage are present just proximal to the epiphyseal cartilage, in some in contact with the cartilages, in others slightly separated. In the other lesions these rounded projections are made up of spongy bone.

In many respects the acute changes resemble infarcts, in their shape, location and more than anything else in the character of the alterations—necrosis with hemorrhage. We have not as yet discovered any obstruction to vessels or other signs of embolism and it should be borne in mind that hemorrhages here will result in infarction or alterations closely resembling infarction. The occurrence of early and late changes in Animal XVI previously referred to, the acute changes

in the rib, the chronic changes in the radius, indicates that the hemorrhages did not occur in the parts affected at the same time. However, in the preparations so far examined it has not been possible as yet to detect early and late changes in the same costochondral or epiphyseodiaphyseal junction.

May 11, 1914.

TWO UNUSUAL INTERNAL HERNIAS—ONE INTERSIGMOID, THE OTHER INTO THE PARA-DUODENAL POUCH OF LANDZERT

FRANK NUZUM AND JOHN NUZUM

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The following reports are made because of the relatively few examples of carefully studied internal hernias of the abdomen:

Intersigmoid Hernia.—If the sigmoid flexure of the colon is drawn upward to the right, the under surface of the mesosigmoid which is thus exposed presents in a considerable number of bodies examined a small peritoneal pouch. This pouch is situated at the line of attachment of the mesosigmoid to the abdominal wall and just about the point of emergence of the left iliac artery from beneath the mesentery of the sigmoid colon. The orifice of this pouch, the intersigmoid fossa, varies from 1 to 4 cm. in diameter and its edges may consist of a sharply defined peritoneal rim or of only a rounded margin, the fossa in this instance being represented by but a slight depression. The sigmoid vessels are often found close to the inner and upper edge of the orifice. The pouch lies behind the sigmoid mesocolon, is directed upward and its length varies from 1 to 10 cm., the fossa having been described as extending upward to the middle of the kidney or to the tail of the pancreas. Often through the posterior wall of this sac the left ureter can be seen where it crosses the iliac artery.

Variations from the usual form and position of the fossa have been recorded. The fossae may be multiple.

Machol[1] reported an instance in which there were three separate fossae; Gruber and Waldyer[2] two fossae; Brosike[3] four separate fossae, and Hensing and Gruber[4] one, which had a single orifice with two branches.

The percentage of bodies in which the intersigmoid fossa is present varies considerably with the several writers on this subject. Gruber[5] gives it as 52 per cent., Moynihan[6] as 70 per cent., and Treves[7] as 84 per cent. This variation is due chiefly to the age of the bodies examined, the fossa being almost invariably present in infants and tending to disappear with advancing years. This disappearance is the result of processes of thickening and adhesion in the mesosigmoid, which take place as an individual grows older, so that in the third decade it is often entirely absent.

The hernia under consideration was found in the body of a man whose death was not in any way connected with the hernia or with any process of disease in the abdomen. The following record was made at the time by Dr. E. R. LeCount, who conducted the post-mortem examination:

"On opening the abdomen and reflecting the omentum up over the thorax, the small bowel is found in a sac formed by the dislocation of the descending colon to the right, an adventitious mesocolon (see Fig. 1). The entire small bowel is in this sac, having passed in through a hernial ring located close to the ileocecal valve, apparently in the mesosigmoid, which also is far over to the right. It seems to me that the gradual filling up of this sac by the small bowel has brought about dislocation of the descending colon and mesosigmoid to the right as well as the production of an adventitious mesocolon (see Figs. 1 and 2).

"This last is not adherent to the abdominal wall in front. The small bowel is therefore contained in a sac formed almost entirely of mesocolon and mesosigmoid for, after passing through the mesentery of the sigmoid, the small bowel

1. Beiträge zur Kenntnis der Hernia intersigmoidea, Beitr. z. Klin. Chir., Tubing, 1911, lxxvi, 209.
2. Hernia Retro-peritonealis, nebst Bemerkungen zur Anat. d. Perit., Breslau, 1868.
3. Ueber Intra-abdominelle Hernien und Bauchfelltaschen, Berlin, 1891.
4. Zur Hernia Interna, St. Petersburg Med. Ztg., 1861, p. 1.
5. Reference as above.
6. Retro-Peritoneal Hernia, New York, 1906.
7. Surgical Applied Anatomy, New York, 1911, p. 407.

pushed the point of attachment of the descending colon to the left wall of the abdomen upward and to the right, as well as pushing to the right the mesentery forming the hernial opening. As the descending colon and its mesentery were

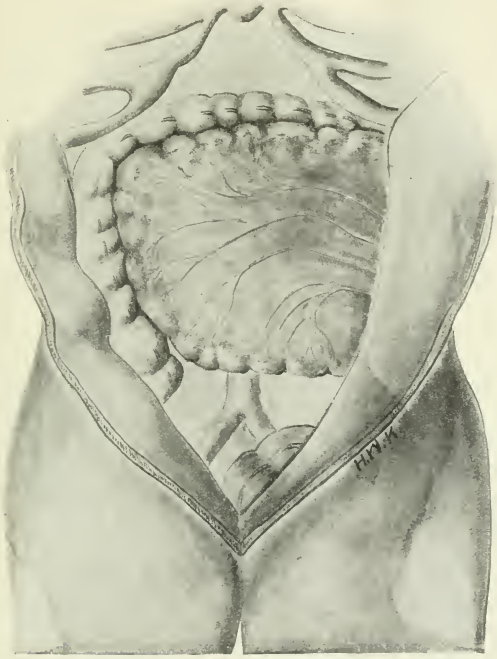

Fig. 1.—The hernial sac lies under an adventitious or newly formed mesocolon relatively thin, with many blood-vessels and made by dislocation of the descending colon and sigmoid to the right as the sac filled—from sketch made at the post-mortem examination.

pushed to the right by the small bowel getting through the opening in the mesosigmoid and to the left of the mesentery, there went over to the right with the descending colon a

layer of peritoneum, pulled away from the lateral wall by gradual stretching and lengthening crosswise of the abdomen; a new adventitious mesentery. This layer forms the front wall of the sac; the real mesentery forms its back and right walls. The sac is lined with peritoneum and con-

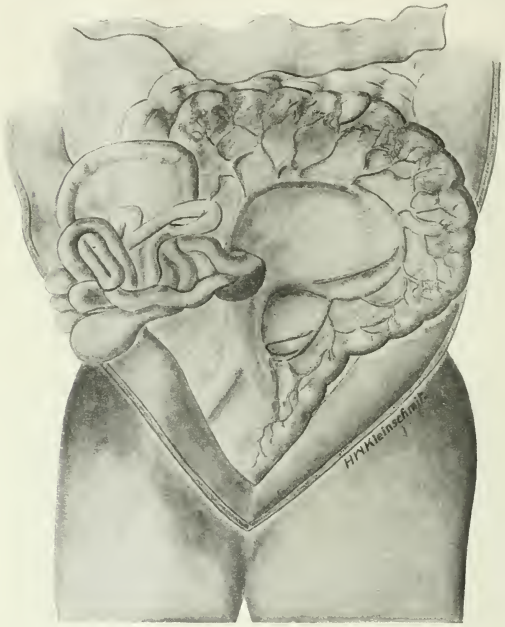

Fig. 2.—The dislocated descending colon and sigmoid are turned up and to the left, exposing the opening into the hernial pouch. The bowel is partly pulled out—from sketch made at the post-mortem examination.

tains nearly the entire mesentery of the small bowel. Neither the sac nor the hernial opening are in any way connected with the duodenojejunal pouch."

The small intestine, having passed through the opening described above, came to lie to the left of the sig-

moid colon, and as more and more of the bowel came to occupy this space it worked upward and into the intersigmoid fossa, gradually distending this pouch until a large part of the small bowel was contained within it. The opening into this intersigmoid fossa is a circular orifice 8 cm. in diameter. Its edges are not thickened and contain no large blood-vessels. The sac is lined with a smooth, glistening serous membrane.

As before stated, it contained nearly the entire small bowel and its mesentery, only approximately 20 cm. of the proximal portion of the jejunum and 30 cm. of the distal end of the ileum lying without the sac free in the abdominal cavity. The small bowel was withdrawn from the sac without difficulty and its loops were free and without any evidence whatsoever of strangulation.

It is believed that this is a true instance of intersigmoid hernia: first, because the position of the hernia and the relation of the hernial sac to the abdominal contents were such as are described in conditions of intersigmoid hernia; second, because the mesosigmoid was displaced to the right in a manner typical for intersigmoid hernia; third, the anterior wall of the sac was formed by a layer of peritoneum stretching from the mesosigmoid to the left lateral abdominal wall; fourth, because the hernial sac was lined with peritoneum.

On reviewing the literature, we have succeeded in finding reference to five other examples of intersigmoid hernia.

The first authentic instance is that of F. S. Eve,[8] recorded in 1885, the specimen being still preserved. A detailed description is given as follows:

"On opening the abdomen I found the following condition: The intestines were injected and distended with flatus, but there was no effusion of lymph. On moving them aside to the right it was observed that the sigmoid flexure was displaced toward the midline and extending from its posterior surface toward the left iliac fossa was a sheet of peritoneum, through an opening in which a knuckle of small bowel passed.

8. A Case of Strangulated Hernia into the Fossa Intersigmoidea. Brit. Med. Jour., 1885, p. 1195.

The protruded intestine was withdrawn without the least resistance, and proved to be a portion, about 6 inches in length, of the lower end of the ileum. It was moderately congested, and was marked at each end by a slight constriction.

"The opening in the peritoneum was oval, and its long diameter measured one-half inch. It was situated close to the left side of the sigmoid flexure, its lower margin being from 1 inch to 1.5 inches above and to the outer side of the sacro-iliac synchondrosis, and 1 inch from the ovary. On dissecting up the peritoneum from the subjacent muscles, the opening was found to lead into a sac of subjacent peritoneum having very thin walls, which were attached to or continuous with the margins of the opening. The sac was pyriform, measured 3 inches in its long diameter and extended upward and backward beneath the large intestine. Its posterior surface, in contact with the iliacus and lumbar muscles, was easily dissected from its connections, but its anterior surface was so closely connected with the peritoneum and posterior surface of the large bowel that its continuity in parts could not be established.

"The sigmoid flexure was nearly surrounded by peritoneum, but had not a distinct mesentery, the two layers of peritoneum reflected from it being nowhere in contact."

A post-mortem examination was held, but no definite information regarding the herniation is recorded in the protocol.

In 1897, Lambret[9] recorded an instance in which a man, 63 years old, was seized with sudden pain in the abdomen following an attempt at defecation. A laparotomy was performed and on opening the abdomen "one sees a portion of the intestines dilated, the other portion collapsed and empty. The hand of the operator encounters, in the upper part of the left iliac fossa, an indurated, smooth kidney-shaped tumor, the exact nature of which it is difficult to say at once. The point of division between the dilated and collapsed portion of the intestine is sharply demarcated, and it is evident that the obstruction lies at the junction of the collapsed and distended portions of the small bowel. With moderate traction, which is necessary, one brings to view a sharply folded loop of bowel, the two ends

9. A propos du troisième cas connu de hernie dans la fossette intersigmoide, L'Echo Medical du Nord 1897, p. 325.

lying parallel like the barrels of a gun. This loop is edematous, violaceous and dull, but does not present any line of constriction. The caliber of the intestine is patent as soon as the fold is removed. The tumor which was noted at the beginning of the operation has disappeared. The hypothesis that this is a hernia into the intersigmoid fossa is strengthened on finding the orifice of this recess the size of a five-franc piece with its margins infiltrated and violaceous. The cavity of the fossa is enlarged, is spherical in shape and is the size of a small orange. Its walls are violaceous and it contains a quantity of a sanguineous exudate.[10]

On the day following this operation a colotomy was done, but the patient died. A post-mortem examination revealed a marked peritonitis.

Coley[11] has published the results of a post-mortem examination on the body of a baby dying from intestinal obstruction on the third day after birth. The small bowel was found entirely concealed in a large hernial sac lying on the left side of the vertebral column with its mouth over the left sacro-iliac synchondrosis. The small bowel was comparatively easily withdrawn from the sac, which was lined with peritoneum. The position of the sigmoid flexure is not stated. The author concludes that this is an example of intersigmoid hernia and the first reported in an infant.

Krall[12] has recorded a unique instance in which a portion of the sigmoid colon itself was looped over and caught in the recessus intersigmoideus. It is probably possible for only the under portion of the sigmoid to be caught in this manner.

Machol[13] has described the fifth and final example of intersigmoid hernia. It was found in a male patient, 66 years old, suffering from acute intestinal obstruction. On operation, 30 cm. of the small intestine beginning at a point 50 cm. above the ileocecal

10. The above is a translation of a portion of the original article.

11. Strangulated Retroperitoneal Hernia of the Intersigmoid Fossa, Ann. Surg., 1909, l, 238.

12. Ein Beitrag zur Kenntnis der Hernia Intersigmoidea. Deutsch. Ztschr. f. Chir., Leipzig, 1911, cx, 303.

13. Beiträge zur Kenntnis des Hernia Intersigmoidea, Beitr. z. klin. Chir., Tubing, 1911, lxxvi, 209.

valve was found held within the grasp of the fossa intersigmoidea. The bowel was withdrawn without necessitating any cutting of the constricting orifice. The patient died. Necropsy revealed the presence of three recessi intersigmoidiae, the bowel having been retained in the upper and larger of the three.

The correct conception of the origin of this fossa was first given by Toldt[14] and later confirmed by Symington[15] in 1892. In early fetal life the descending colon possesses a long mesentery which is attached to the posterior abdominal wall near the midline of the body. By the seventh month, this mesocolon is absent and the descending colon lies in the position in which it is found in the adult. It was thought that during the growth of the body the two layers of the mesosigmoid were spread apart and came to line the posterior abdominal wall. Toldt and Symington have shown, however, that such is not the case. If transverse sections are made through the abdomen of a six or seven months' fetus and the descending colon grasped and pulled upward and to the right a stripping process occurs whereby the mesentery of the descending colon is reformed and yet the parietal peritoneum still retains its position. In Toldt's language, there has been a "physiological adhesion" between the peritoneum on the left side of the mesosigmoid and that lining the left posterior wall of the abdomen. If a fine probe is passed into the sigmoid fossa and the colon then stripped up, the probe will be exposed lying behind the mesocolon and in front of the parietal peritoneum.[16] This process of "physiological adhesion" begins first in the region of the splenic flexure of the colon and travels downward. The prominence of the kidney gives rise to a groove at its inner margin which does not allow the parietal peritoneum and the peritoneum of the mesentery to come into apposition readily, wherefore adhesion does not occur and a fossa remains. The lower portion of this groove never

14. Bau und Wachsthumsveränderung der Gekröse des menschlichen Darmkanales. Denkschrift d. k. Akad. der Wissensch., Wien, 1872, (xv).

15. The Relations of the Peritoneum to the Descending Colon, Jour. Anat. Phys., 1892, 2v, 530.

16. Retroperitoneal Hernia, Moynihan, London, 1906.

permits complete adhesion and "opening below at the back of the sigmoid mesentery is the fossa intersigmoidea." Irregularities in this fusion easily explain the variations of the fossa previously referred to.

From the foregoing accounts, it is evident that the clinical symptoms of herniation into the intersigmoid fossa vary markedly. There may be none whatsoever, as illustrated by our example, or there may be acute obstruction followed by peritonitis (Lambert's instance). Because reports of intersigmoid hernia are so few and because the symptoms in these have been so diversified, it is doubtful if a positive clinical diagnosis of this condition can be made without operation.

Moynihan, in his extensive consideration of this type of hernia, cited but two: the first that of Eve, given above; the second, that reported by McEchles, and regarded by later writers as only an inguinal hernia reduced en masse. In Eve's example and in the remainder, excepting Kroll's, the small bowel occupied the intersigmoid fossa; in the latter, a portion of the sigmoid colon itself occupied the fossa. Our instance differs from all of the others in the manner in which accessibility to the mouth of the intersigmoid pouch was gained. The small intestine first came to lie on the left side of the sigmoid colon by passing through an opening in the mesosigmoid. In the others (excepting Kroll's report), the small bowel passed between the sigmoid mesocolon posteriorly and the anterior abdominal wall in front, thus gaining access to the fossa.

It is noteworthy that in spite of the etiologic factors for strangulation present in our example, so far as is known no symptoms of such a condition were ever experienced.

Left Duodenal Hernia.—If the great omentum together with the transverse colon are lifted upward and reflected back over the thorax, by making gentle traction on the jejunum at the duodenojejunal flexure, a delicate peritoneal band containing a few muscle fibers is seen passing from the flexure to fix the bowel to the parietal peritoneum. This constitutes the suspensory ligament of Treitz. Just behind it lies the

superior duodenojejunal fossa, which is present in approximately 40 per cent. of bodies (Fig. 3). Its apex extends upward toward the body of the pancreas; its orifice looks downward opposing the mouth

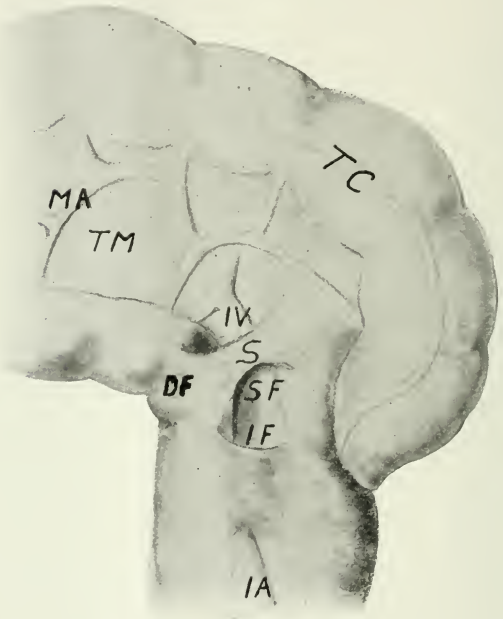

Fig. 3.—Illustrating the normal anatomical relations about the duodenojejunal junction. (Modified from Davis, Applied Surgical Anatomy, Philadelphia, 1913.) (S) Suspensory ligament of Treitz. (SF) Superior duodenal fossa. (IF) Inferior duodenal fossa. (IV) Inferior mesenteric vein. (DF) Duodenojejunal flexure. (TC) Transverse colon. (MA) Middle colic artery. (TM) Transverse mesocolon. (IA) Inferior mesenteric artery.

of second pouch known as the inferior duodenojejunal fossa of Treitz.

This second pouch is found in about 70 per cent. of all adult bodies and lies opposite the third lumbar vertebra on the left side of its body. It has been the universal but erroneous belief that all of the so-called "duodenojejunal" hernias have their origin in this pouch.

Still a third definite pouch of this region was described by Landzert[17] in 1871, a fossa bounded on the right by the root of the mesentery of the small bowel, on the left by a fold containing the inferior mesenteric vein, and below by the "mesenterico-mesocolic" fold. The parietal peritoneum, the aorta, psoas muscle, renal vessels, ureter, and often a part of the anterior aspect of the left kidney lie behind this pouch. The position and size of the mouth of the sac, when herniation of the bowel into it occurs, naturally vary according to the amount of bowel contained. The orifice of the sac looks downward and slightly to the right. This is known to-day as the paraduodenal fossa of Landzert. Variations from the normal are common. In fact, this pouch so often exists with other pouches that no little confusion has at times developed concerning it. It is highly essential that the inferior mesenteric vein be found in the orifice of the sac and in the superior boundary of the hernial sac, arching upward and to the right over the pouch to predicate hernia into it. Along with the vein the left colic artery or branches of this vessel can be found in the root of the descending colon on the left side of the pouch. This paraduodenal fossa is seen most frequently in the new-born or the fetus. Hernia into this pouch rarely becomes incarcerated.

In the instance reported here, death was in no way concerned with the hernia.

John H., a laborer, aged 40 years, was admitted to the Cook County Hospital on Jan. 15, 1913, and died on the following day, Jan. 16, 1913. The clinical diagnosis of alcoholism and delirium tremens was made. Necropsy revealed the presence of a bronchopneumonia, marked edema of the brain, gangre-

17. Ueber die Hernia retroperitonealis, und ihre Beziehungen zur Fossa duodeno-jejunalis, St. Petersb. med. Ztschr., 1871, n. F., 306. St. Petersburg, 1872, cited by Moynihan.

nous cystitis, together with an ascending cystoureteropyelonephritis.

The following record was made at the post-mortem examination:

On opening the peritoneal cavity a globular mass is seen (Fig. 4) below and behind the cardiac end of the stomach; in size slightly larger than two closed fists, and composed of approximately the proximal half of the small bowel covered by a thin membrane. At first sight its appearance

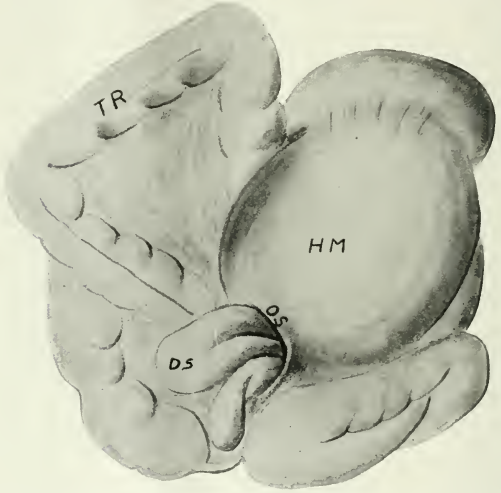

Fig. 4.—Illustrating the appearance of one of the larger types of left duodenal hernias. (Modified from the illustration in Moynihan's work of conditions illustrated by Treitz.) (OS) Orifice of the sac. (HM) Hernial mass. (DS) Distal portion of the ileum protruding through the mouth of the sac. (TR) Transverse colon pulled over to the right side.

suggests an aggregation of loops of small bowel bound together by adhesions such as are sometimes encountered in the healing of a peritonitis. The colon, adherent to the mass, is carefully dissected free as far as the ileum, the distal half of the small bowel freed from the mesentery, when it is seen that the proximal half of the small bowel is being

gradually reduced through the orifice of a duodenojejunal pouch. The ring through which the bowel entered is circular and readily distensible, measuring 6 to 10 cm., according to the amount of distention exerted. This circular ring is formed on its right side by the upper part of the base of the mesentery of the small bowel, on the left by the root of the mesentery, which is present and is attached to the descending colon, and on the upper border by a fibrous band extending between the mesentery of the small bowel and that of the colon, which transmits an artery supplying the mesentery of the descending colon and appears to consist of a thickening of the edge of a sac. There is a scar in the root of the mesentery of the small bowel just beyond that portion that goes to form a part of the ring of the sac.

The roof of the sac lies just below and closely adherent to the pancreas. The posterior wall of the sac is in proximity to the anterior surface of the left kidney, with the retroperitoneal tissues and the aorta on its inner side, the aorta forming the right border of the sac. The left ureter passes along the posterior wall of the sac and is adherent to it. The portion of the jejunum just inferior to the duodenojejunal angle can be seen as it passes out of the hernial sac over the inner and inferior edge of the ring. (From the original description by Dr. Le Count.)

From the foregoing account of the relations it seems reasonable to believe that the hernia was into the paraduodenal pouch of Landzert, because its situation and boundaries are in every way similar to those cases of left duodenal hernia recorded in the literature; also because the inferior mesenteric vein and left colic artery were both within the fold of the sac at the orifice, thus constituting that essential so-called "vascular arch of Treitz." Furthermore, had it originated in the inferior duodenal fossa of Treitz, its ring should have contained no vessels.

As regards the origin of these fossae, Moynihan regards the folds forming the same as "fusion folds" between the surface of the ascending portion of the duodenum and the anterior right surface of the descending mesocolon folds, which take their origin from the time when these peritoneal surfaces are in close apposition. Treitz (Hernia Retroperitonealis, ein Beitrag zur Geschichte innerer Hernien, Prague, 1857) stated that they result from the embryonic move-

ment of the intestinal canal, the folds resulting from the dragging of the intestine in the normal displacement or volvulus of the viscera to the right. In fact, he considers them "traction folds." Moynihan raises the very logical objection that even earlier than the formation of these folds, the duodenum at its junction with the jejunum is firmly fixed to the posterior abdominal wall by a small muscular band known as the suspensory ligament and first described by Treitz himself.

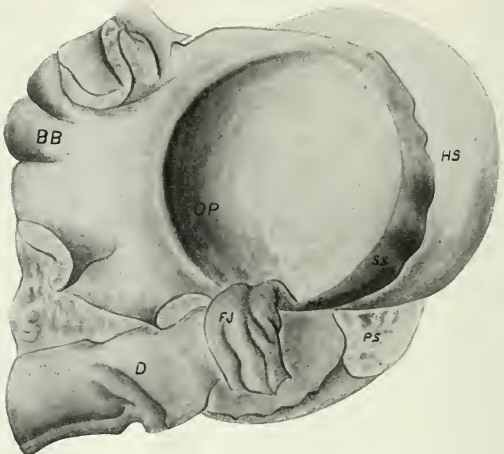

Fig. 5.—Illustrating the conditions in the new case here reported. The proximal portion of the small bowel which was originally contained in the sac has been reduced through the hernial orifice. (OP) Orifice of the hernial pouch. (MF) Mesentericomesocolic fold. (PS) Pancreas in cross section. (HS) Hernial sac. (FJ) First portion of the jejunum. (D) Duodenum. (BB) Base of the mesentery of the small bowel. (SS) Small remaining portion of the mesentery of the sigmoid which forms the left boundary of the hernial ring; here the inferior mesenteric vein was found.

There are two chief varieties of duodenal hernias, namely, (*a*) left duodenal and (*b*) right duodenal hernia. Treitz states that all types originate in the inferior duodenal fossa, while Moynihan contends that

they arise primarily in the paraduodenal fossa of Landzert. However this may prove to be, they both agree that the inferior mesenteric vein can always be seen in the neck of the sac, while the left colic artery may be closely applied to it or at some little distance away. Treitz considers the following as the *essentials* concerned in the production of a duodenojejunal hernia:

1. The existence of a fossa and its boundary fold.
2. The presence of the inferior mesenteric vein in this fold.
3. Sufficient freedom of movement of the small bowel to permit of the introduction of the same into and distention of the fossa. To which may be added:
4. Usually an increased abdominal pressure, which may result from a hypertrophied prostate, phimosis, chronic bronchitis, etc.

The size of the hernia varies naturally within a wide range—from a diameter of a few centimeters to that of an adult head. The amount of bowel involved varies from a few inches to the entire extent of the small intestine; in other words, from the flexure to the ileocecal valve. Although, as previously stated, the folds and fossa are best developed in children, nevertheless the majority of hernias reported have occurred in adult people. The orifice (ring) of the sac is situated, as a rule, at the back of the hernia and close to the lumbar vertebrae. But its exact location as regards the hernial mass will depend almost entirely on the amount of bowel contained within. The average diameter of the neck has been estimated at 6 cm. The orifice of the sac is bounded posteriorly by the peritoneum of the posterior abdominal wall, while the upper, anterior, and lower boundaries of the opening are formed by the edge of the peritoneal fold containing the inferior mesenteric vein, the "plica venosa." According to Moynihan, the left colic artery is usually closely applied to the vein throughout the whole of the anterior portion of the fold, but above, the artery turns to the left while the vein arches boldly to the right.

There have been approximately seventy authentic cases of left duodenal hernia recorded in the literature up to 1914.

As a general rule, duodenojejunal herniae are found at necropsy. Of all those reported, in but ten was the hernia the direct cause of death (acute intestinal obstruction). In addition, those cases where the hernia has been found to be strangulated are usually of the right duodenal type.

It is indeed interesting to learn that even in a pathologic condition as rare as this, one case was correctly diagnosed during life by Staudenmayer. And, again, in the case reported by Barr (right type) the appearance of the abdomen was so striking that a drawing was made of it as the body lay on the table before necropsy. Accordingly, Moynihan has justly gone so far as to formulate a syndrome for the probable diagnosis of duodenojejunal herniae—"the circumscribed globular distention of the mesogastrium, retraction of the epigastric region corresponding to the colon, the presence of a rather tense, elastic mass to be distinctly felt and outlined, giving somewhat the impression of an ovarian cyst and extending from the mesogastrium to the left, the fact that this tumor mass yields a tympanitic note on percussion with gurgling intestinal sounds on auscultation." Also the presence of hemorrhoids and bleeding from the rectum perhaps, resulting from compression of the inferior mesenteric vein. All these facts when considered in conjunction with a history of chronic constipation or slight digestive disturbances should strongly suggest the diagnosis. To recapitulate briefly:

1. A definite localized, palpable and resonant tumor mass occupying a definite region of the abdomen—slightly movable but fixed during respiration and varying in size from a child's head to a nine months' pregnancy.

2. On auscultation distinct gurgling sounds may be heard anywhere over the mass.

3. Perhaps a history of chronic slight digestive or intestinal disturbances.

4. Often a venous stasis or actual bleeding from the rectum, resulting from compression of the inferior mesenteric vein in the neck of the hernial sac.

The literature reports but nine successful operations, namely, eight of left and only one of right duodenojejunal hernia. Undoubtedly, we may best understand the method of procedure together with the difficulties encountered in the treatment of these herniae from a study of the report by Lawford Knaggs,[18] which follows:

John R., aged 22, a laborer, fell from a scaffolding and was severely injured. Taken to a hospital and a compound fracture of the humerus was reduced. The patient began to fail rapidly. An exploratory laparotomy was performed and a left duodenojejunal hernia discovered. This hernial mass measured 8 inches in its greatest diameter; the orifice of the sac was 3.5 inches in width. On carefully reducing, the small bowel contained some lymph and fibrin, while the serous coats of the small intestine had lost their glistening, shiny appearance and were of a dull gray hue. Evidently they were dealing with an inflamed hernia. After reduction, the sac was obliterated by packing with sterile cotton and the orifice closed by superficial sutures. The patient suffered from surgical shock—was given 2½ pints of normal salt solution. Perfect recovery. Died nine months later of typhoid fever. Necropsy confirmed the diagnosis.

In the majority of cases, the strangulated bowel can be easily withdrawn from the hernial sac. And this is most fortunate, since the neck of the sac cannot be enlarged without severing the inferior mesenteric vein. Still, in one case operated on the vein was found to be thrombosed and a collateral venous circulation had been established. If it is found impossible to reduce the bowel, the sac may be entered through an incision to the outer side and external to the vein, portions of the intestine are then withdrawn, incised, emptied of their contents, closed by careful invagination with sutures and replaced and then the intestines can be readily reduced through the ring. The difficulty of satisfactorily closing the hernial orifice arises from the fact that the sutures will necessarily puncture or constrict the encircling vascular loop unless placed very superficially.

May 11, 1914.

18. A Case of Inflamed Duodenal Hernia, Brit. Med. Jour., 1905, ii, 1449.

METASTATIC CALCIFICATION *

H. GIDEON WELLS

There are some thirty-one cases of this condition adequately described in the literature. Its chief importance lies in the light it throws on the method of transportation of calcium in the blood, and the importance of the carbon dioxid in this process. This report concerns a typical case occurring in a young man with myelogenous leukemia. The striking feature was the extensive deposition of calcium in the endocardium of the left auricle and also in the left ventricle. The lung showed universal deposition of calcium in the alveolar walls, and also in the pulmonary veins. The coronary arteries were extensively infiltrated. There was no calcification in the right side of the heart or in the branches of the pulmonary arteries in the lungs. This distribution of the calcium deposits shows, as by a natural experiment, the importance of carbon dioxid in the solution of calcium in the blood. When bone is being rapidly absorbed, as in leukemia, the venous blood carries the calcium salts up to or near the saturation point. When the blood loses its carbon dioxid in the lungs the calcium at once precipitates, as a mixture of phosphate and carbonate, in the alveolar capillary walls, the pulmonary veins, and even further along in the left auricle and ventricle and in the coronary arteries.

November 9, 1914.

* The complete article will be published in the Arch. Int. Med.

TRANSACTIONS OF THE CHICAGO PATHOLOGICAL SOCIETY

VOL. IX. MARCH 1, 1915. NO. 6

FATAL MALARIA DUE TO THE TERTIAN PARASITE

FRANK BILLINGS AND WILBER E. POST

The patient, a man of 50 years, was brought to the Presbyterian Hospital in a delirious condition. He was very fleshy, markedly jaundiced, with pale lips. There were no paralyses nor disturbances of reflexes The blood contained 44 per cent. hemoglobin, 3,520,000 red and 12,550 white cells. When drawn, the blood was chocolate brown and contained numerous plasmodia of tertian malaria of all stages from the non-pigmented and pigmented coarse rings to the sporulating forms. No crescents were found. Quinin bisulsulphate was administered subcutaneously, but the patient became progressively worse and died about twelve hours after admission.

An autopsy was held about ten hours after death by Dr. Peter Bassoe, from the record of which the following abstract has been prepared:

ANATOMIC DIAGNOSIS

General icterus; general anemia; chronic and acute splenitis; acute degeneration and pigmentation of liver; fatty degeneration of kidneys; diffuse bronchitis; pulmonary edema; hypostatic congestion of left lower lobe.

The spleen weighs 660 grams and is fairly firm. The capsule is smooth and dark greenish-brown. The cut surface is dark brownish-gray. The pulp is swollen and prominent. The Malpighian bodies are indistinct; the trabeculae can be made out.

The liver weighs 1,920 grams. It is soft, smooth and dark greenish-brown; the cut surface is of a uniform greenish-brown color; the lobular markings are indistinct. Where

they can be made out the centers appear dark brown, the outer portions of a grayish-green color. The gall-bladder and ducts show no changes.

The brain presents no external changes.

HISTOLOGIC STUDY BY THE AUTHORS SHOWED THE FOLLOWING:

Brain.—In the left frontal lobe, cerebellum (Fig. 1), medulla spinalis and motor areas of left cortex (Fig. 2), were found intracapillary masses of swollen, infected red corpuscles, free parasites and masses of pigment. The plasmodia were for the most part well developed and many sporulating forms were found. An apparently older thrombus in a capillary of the left olivary body was composed of masses of free, well developed parasites. The red blood

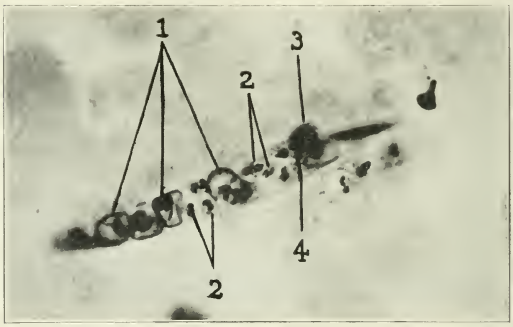

Fig. 1.—Cerebellum. Showing recent thrombus in capillary—× 1000. 1. Red cells containing plasmodia. 2. Plasmodia free in capillary. 3. Nucleus of endothelial cell in wall of the capillary. 4. Pigment in center of segmenting plasmodium.

corpuscles had been destroyed. A cortical cell in the left motor region of the cerebrum showed a portion of the cytoplasm in which the chromatin of the Nissl bodies had degenerated into a fine powder-like mass. A similar tigrolysis was found in the Purkinje cells of the cerebellum, while some ganglion cells in the nucleus ambiguous of the medulla spinalis show the Nissl bodies well preserved.

Spleen.—Showed evidence of both a chronic and an acute process. Pigmentation was more marked at the periphery of the Malpighian corpuscles. Under higher magnification (Fig. 3) the enlarged blood sinuses showed a few of the

red cells infected and an occasional extra-cellular parasite. The lymph sinuses contained large numbers of free parasites, a few infected red cells and numerous large phagocytic endothelial cells containing various sized masses of pigment, an occasional shadow of a red blood corpuscle as well as an occasional parasite. These large masses of pigmented cells corresponded to those described by Ewing[1] and are due not to an elaboration of the malarial parasite, but to a globulocidal action of the plasma upon the red blood corpuscles. They are "more often distinctly crystalline, and large, spheroidal, homogeneous black grains," while those of the malarial parasite are "fresh yellowish finely granular."

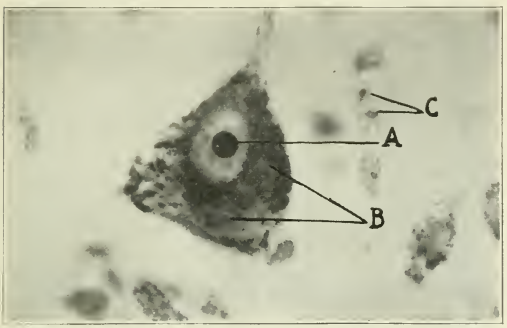

Fig. 2.—Cortical cell with axone, in left motor region of cerebrum showing advanced tigrolysis—× 1200. A. Nucleolus within fairly well defined nucleus. B. Portion of cytoplasm showing chromatin of Nissl bodies degenerated into fine powder-like mass. C. Plasmodia within small capillary.

Kidney.—No compact thrombus masses of parasites were found in the vessels of the kidney, but single infected red blood cells were numerous in the intertubular and glomerular capillaries. Masses of coarser pigment in phagocytic endothelial cells were also quite frequent, especially in the vessels of the medulla of the kidney. A few parasites were found free within Bowman's capsule. This would account for the finding of parasites in the urine reported by some and we regret that a search of the urine was not made in this case. The tubules of the kidney show marked degeneration of the

1. Jour. Exper. Med., vol. vi, p. 151.

renal epithelium. Fatty degeneration was not a feature of the sections examined, although special staining for the same was not done.

Liver.—Section showed areas of degeneration, even points of necrosis. The usual pigmentation was present. The most unusual feature was in the large number of phagocytic endothelial cells and plasmodia within the vessels. Figure 4 shows pigment within the liver cells.

Pancreas.—The parenchyma cells of the pancreas were distorted, due to an error in the use of the fixing fluid, but

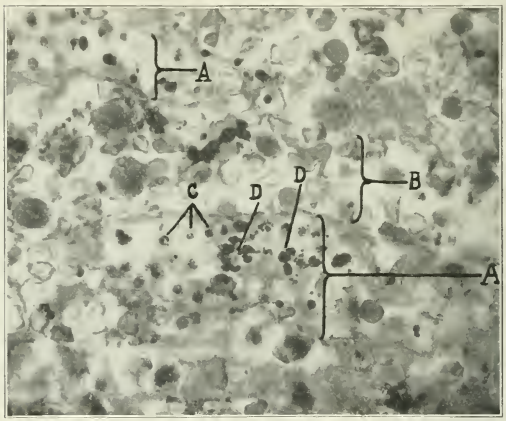

Fig. 3.—Spleen—×900. A. Lymph sinuses. B. Blood sinus. C. Plasmodia free in lymph sinus. D. Masses of pigment within phagocytic endothelial cells.

sections show masses of malarial parasites within the capillaries.

Lung.—Sections were made through the portion of the lung involved by hypostatic consolidation. Capillaries of the alveolar walls contained intact and infected red blood corpuscles.

Heart.—Sections through the wall of the left ventricle showed numerous infected reds and free plasmodia within the capillaries although no masses resembling thrombi were found.

Prostate.—Parasites were found within the capillaries of the prostate similarly as in other tissues.

Bone Marrow.—Neither smears nor sections were preserved.

This case calls our attention to certain clinical and pathological features:

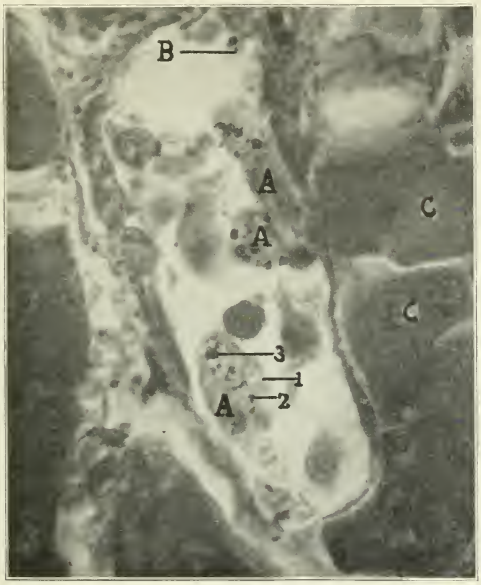

Fig. 4.—Liver, showing small branch of vena centralis—× 1200. A. Enormous phagocytic endothelial cells containing: (1) Red blood corpuscles. (2) Malarial pigment. (3) Plasmodium. B. Plasmodium free in vein. C. Liver cells, within which are fine yellowish brown pigment granules as well as coarser pigment masses.

1. The only parasite found in our search in blood and tissues was the plasmodium of tertian malaria. Various Italian authors of wide experience believe that malaria is not fatal when due to the tertian para-

site alone. But Ewing[2] reports one in which no other parasite was found and also refers to another in which only one crescent was found after long search while tertian parasites were numerous. Barker[3] reports a case of profound tertian infection in which, however, death was referable to a general infection with streptococcus pyogenes. Our own case showed the typical, terminal features of fatal malaria — normal temperature, prostration, rapid respiration, the mental exhaustion or delirium frequently witnessed in profound anemias followed by coma.

2. The thrombi of malarial parasites in the capillaries of the brain were for the most part of recent formation. This may account for the fact that the coma in this case was of short duration, although this must not be interpreted to mean that cerebral thrombosis is essential to the occurrence of coma in malaria. Cerebral symptoms in fatal malaria may be due to anemia plus the toxic effect of the infection. Local massing of parasites in the vessels within the heart muscle was noted in a case reported by Ewing, and to this fact was attributed the prominence of cardiac symptoms. It is to be noted, however, that this patient had suffered periods of broken compensation at different times for several years. Acute degeneration of the kidneys can usually be explained only by the toxic effect of the infection. In one of Ewing's cases acute hemorrhagic nephritis was diagnosticated and microscopic examination of the kidney showed marked degree of filling of the capillaries by malarial parasites. The occurrence of thrombi of parasites in any one organ seems therefore to aggravate symptoms arising from disturbance of that organ.

3. While actual thrombi of parasites were found only in the brain of our case, there was a distribution of many plasmodia in the capillaries of all of the tissues examined. In this particular the findings differ from those usually described. Their ready demonstration may be due to the method of staining — Mann's eosinmethyl blue.

2. Jour. Exper. Med., vol. vi, p. 141.
3. Johns Hopkins Hosp. Rep., 1905, v.

4. It is of clinical importance to emphasize the diagnostic significance of the peculiar chocolate-brown color of the blood as it is obtained for the usual blood count as above stated. This is observed in our experience in cases of severe malarial infection and in chronic poisoning by coal-tar derivatives.

REPORT OF A CASE OF OXYCEPHALY OCCURRING IN AN INFANT

GEORGE S. MATHERS

(From the Pathological Laboratory of Cook County Hospital, Chicago.)

Baby L., a white female infant 3 weeks old, entered the Cook County Hospital, May 2, 1914, to the service of Dr. Grulee, with symptoms of malnutrition and a peculiar deformity of the head. The mother said that the cephalic deformity was noticed at birth and since birth the infant had failed to gain weight. The pregnancy was normal and labor was easy. The mother has had one miscarriage and one other child which died in infancy. The family history was negative with the exception of the mother, who was suffering from atrophic cirrhosis of the liver.

Physical examination revealed a poorly nourished infant who seemed quite uncomfortable. There was no cyanosis or dyspnea. The head was rather singularly misshapen. The forehead was very high and the vertex sloped acutely from the bregma, both anteriorly and posteriorly. In the region of the occipital protuberance there was a large walnut-sized bony prominence. The temporal regions bulged outward and downward. The anterior fontanelle was quite large, and the metopic suture was open. The posterior fontanelle and sagittal suture were closed. There was a marked exopthalmos. The pupils were regular and equal and they reacted very slowly to light. There was a slight deviation of the nose to the right side. The palate was arched and there was a slight cleft posteriorly. The intercostal, axillary and posterior cervical lymph glands were enlarged. There was a faint systolic blowing murmur to be heard over the precordium. The liver and spleen were palpable. The extremities were normal.

On entrance to the hospital the infant weighed 4 pounds and 10 ounces. The urine and stools were negative. The blood examination revealed 3,350,000 erythrocytes, 60 per cent. hemaglobin, 9,100 leukocytes, 69 per cent. of which were

polymorphonuclears, 26 per cent. small lymphocytes, 4 per cent. large lymphocytes and 1 per cent. eosinophils. The cerebrospinal fluid was under slight pressure but otherwise negative. The Wassermann and Lange colloidal gold tests were negative. An ophthalmoscopic examination was made by Dr. E. V. L. Brown, who found a moderate primary optic nerve atrophy more marked on the left side. Also on the left side there was some regression of the nerve head. Radio-

Fig. 1.—Photograph of infant during life.

graphic examination of the head revealed the characteristic "digital markings" of oxycephaly. The sella turcica was normal.

Clinically there was nothing noteworthy except the failure of the infant to gain weight until May 13, 1914, when she became dyspneic and cyanotic. These symptoms rapidly increased and she died May 5, 1914. The temperature varied

between 97 and 99.6 F. per rectum. The weight decreased from 4 pounds 10 ounces to 4 pounds 6 ounces at death.

Anatomic Diagnosis.—Marked bilateral disseminated bronchopneumonia; marked dilatation of the right auricle of the heart; passive hyperemia of the lungs, liver, kidneys and spleen; marked emaciation; exostosis of the occipital bone; oxycephalic deformity of the head; persistent metopic suture; patent ductus arteriosus (Botalli); hyperplasia of the tracheobronchial, mesenteric and retroperitoneal lymph nodes; slight hypertrophy of the pyloric valve of the stomach.

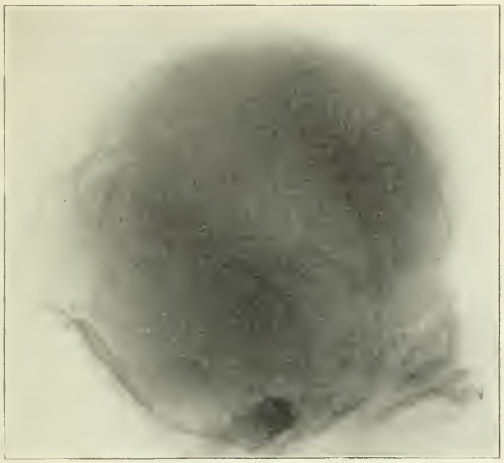

Fig. 2.—Radiograph of the head showing the characteristic "digital markings."

The skull is about normal in size but markedly misshapen. Its general contour is oval with the long axis in the vertical diameter. The vertex is high. In the temporal and occipital regions the bones bulge outward and downward, making the base broader than normal. The metopic suture is open. The anterior fontanelle is open and measures 3.1 cm. in its widest diameter. The posterior fontanelle and sagittal suture are synostosed. With the exception of 1.1 cm. on each side of the fontanelle the coronal suture is

closed. The base of the skull is displaced downward and the fossae are wider and deeper than normal. The sella turcica is unchanged. The orbits are shallow and pyramidal in shape and their axes extend outward and downward. The orbital plate of the frontal bone approaches the vertical rather than the horizontal plane. The face is small and the antri are rudimentary. The hard palate is highly arched. The diameters of the skull are as follows:

	mm.
Length—glabella to inion	104
Length—nasion to inion	101
Base of skull length	57
Greatest breadth of skull	85
Greatest frontal breadth	76
Least frontal breadth	63
Biauricular breadth	67
Greatest occipital breadth	73
Mastoid diameter	68
Height—basion to bregma	102
Height—greatest of the skull	105

The bones of the skull are very thin and more transparent than normal. Ossification is most marked in the bones of the base of the skull. On transillumination numerous circumscribed thinned-out areas can be seen especially in the basilar region. The brain is distorted in shape to correspond to the abnormal cranial cavity. The surface is flattened and compressed. On section the brain tissue is soft and very moist. The ventricles are normal in size and contain a normal amount of cerebrospinal fluid. The only noteworthy gross change in the meninges is the firm attachment of the dura to the bony surface of the cranial cavity.

In an examination of microscopic preparations of the hypophysis and the epiphyses of the long bones no abnormalities were found.

The terms oxycephaly and thurmschadel are synonymous and are used to denote a synostatic skull in which the vertical diameters are greatly increased. Comprehensive studies of this cephalic deformity and the literature may be found in the excellent articles of Euslin,[1] Patry,[2] Fletcher[3] and Herzog.[4]

1. Euslin: Arch. f. Ophthal., Leipzig, 1904, lviii, 151.
2. Patry: Thése de Paris, 1905.
3. Fletcher: Quart. Jour. Med., 1910-1911, iv, 385.
4. Herzog: Beitrag. z. Klin. Chir., 1914, xc, 464.

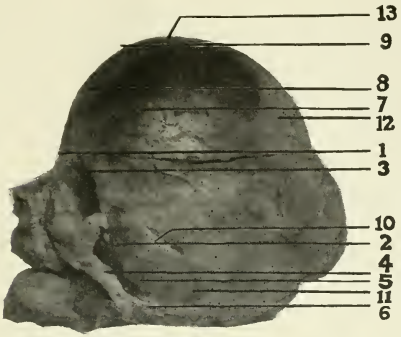

Fig. 3.—Photograph of the skull. 1, bregma; 2, ala magna sphenoidalis; 3, pars orbitalis ossis frontalis; 4, processus zygomaticus; 5, squama ossis temporalis; 6, petrosa ossis temporalis; 7 and 9, ossis frontalis; 8, sutura metopica; 10, fonticulus sphenoidalis; 11, fonticulus mastoideus; 12, ossis parietalis; 13, fonticulus frontalis.

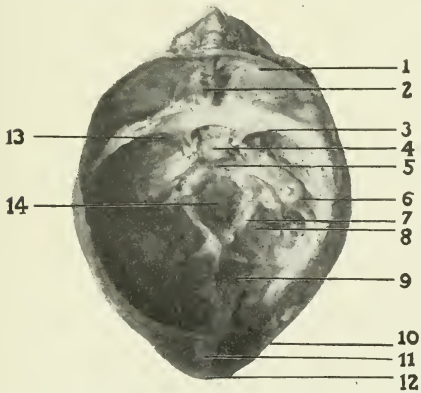

Fig. 4.—Photograph of the base of the skull. 1, pars orbitalis ossis frontalis; 2, crista galli; 3, ala parva ossis sphenoidalis; 4, corpus ossis sphenoidalis; 5, pars basillaris ossis occipitalis; 6, canalis semilunaris; 7, pars lateralis ossis occipitalis; 8, fossa occipitalis inferior; 9, fossa occipitalis superior; 10, squama occipitalis; 11, crista occipitalis externa; 12, protuberancia occipitalis exterra; 13, ala magna sphenoidalis; 14, foramen magnum.

There are about one hundred and twenty-five instances of oxycephaly recorded and about 95 per cent. of these were only observed clinically.

It occurs more commonly in young males and is characterized clinically by an abnormally high head, exophthalmos, optic nerve atrophy of a varying degree and the "digital markings" exhibited in the radiographic examination.

The changes in the skull are constant, and most writers agree that the deformity is due to the premature synostosis of the coronal and sagittal sutures. The growth of the vault is thus restricted in both the anterior, posterior and transverse diameters. The increasing size of the brain is accommodated by an increase in height and width of the skull.

In this instance it seems reasonable to assume that the cephalic deformity was due to the increased intracranial pressure. With the absence of any noteworthy abnormalities in the hypophysis and the epiphyses of the long bones, and in view of the fact that the deformity was present at birth and that there was no gross evidence of hydrocephalus, it furthermore seems reasonable to conclude that the premature synostosis was due to some unknown embryonic disturbance.

Oct. 12, 1914.

MECHANISM OF THE PRODUCTION OF HEMORRHAGIC EROSIONS OF THE ESOPHAGUS AND OF SOME ASSOCIATED LESIONS IN ILEUS

BENJAMIN F. DAVIS

(From the Laboratories of Pathology and of Surgery of Rush Medical College, Chicago.)

Hemorrhagic erosions of the esophagus are among the rarities in the literature of pathology. Three cases are mentioned by Meyer[1] as occurring in infants with melena neonatorum, and Kaufmann reports the occurrence of the lesions in a girl of 17 who died from the

1. Meyer: Inaugural Dissertation, Zurich, 1902.

effects of a severe burn. Diligent search through the available literature has failed to reveal further examples.

According to Kaufmann,[2] hemorrhagic erosions appear in the lower portion of the esophagus as sharply circumscribed patches, from a fraction of a millimeter to a centimeter or more in diameter, more or less oval in outline, sometimes arranged in series, brownish, superficial or invading the submucosa and often in great numbers. The surrounding mucosa may be undermined.

Kaufmann believes that hemorrhagic erosion in the esophagus may arise through the same agencies that are responsible for their production in the gastric mucosa. When small mucous or submucous gastric hemorrhages undergo partial digestion by the gastric juice, so that there results a loss of substance, they become the so-called hemorrhagic erosions. Such small hemorrhages are usually due to passive hyperemia, as in heart diseases, cirrhosis of the liver, pulmonary emphysema, thrombosis, embolism and excessive vomiting.

The evidence in the case to be described seems to offer an explanation of their occurrence which has not been advanced heretofore and which may become worthy of consideration in connection with the operative treatment of intestinal obstruction and with the theory of the relation between toxin production by the intestinal mucosa and death from ileus.

In November, 1911, Dr E. Wyllys Andrews operated upon a man for intestinal obstruction of three days' duration at the Cook County Hospital. At the operation the obstruction was found due to a band of adhesions, about three inches above the ileocecal junction; a beginning peritonitis was also found. The intestine proximal to the obstruction was markedly distended and distally collapsed. The bowel was drained of its contents through an incision which was later closed with a purse-string suture, and an ileocolostomy was done. The patient died a few hours after the operation. At a post-mortem examination, made by Dr. E. R. LeCount, the following anatomic diagnosis was made: Acute serofibrinous peritonitis; laparotomy wound (recently made);

2. Kaufmann: Spezielle pathologische Anatomie, 1909, p. 389.

enterocolostomy; sutured hole in the small bowel; multiple regions of infarction of the small bowel and mesentery due to thrombosis of the mesenteric veins; dilatation of the small bowel; empty colon; large region of red infarction of the liver (Zahn); multiple regions of thrombosis, hemorrhagic infarction and ulceration in the esophagus; marked senile sclerosis of the aorta with atheromatous ulcers and adherent fibrinous masses; healed infarcts of left kidney; marked cloudy swelling and fatty changes in both kidneys; bilateral fibrous pleuritis; marked anthracosis and senile emphysema of the lungs; undescended cecum; hemorrhages into the gastric mucosa.

Of these alterations the ones worthy of special attention are: The dilatation of the small bowel—this was extreme at the time of operation—was relieved by enterostomy, and was again quite marked at necropsy. The areas of thrombosis, infarction and hemorrhage in the mesentery and small intestine—the infarcts, about six in number, were distributed along the course of the bowel, chiefly in the jejunum opposite the mesenteric attachment, as bluish elevations of the mucosa varying in size from that of a silver dollar to oval lesions 4 inches in length; in the central portion of some were narrow slit-like tears in the mucosa about an inch long; the contents of the bowel were bloody. Hemorrhages into the gastric mucosa; these were multiple, varying in size from a millimeter or two to that of a silver dime. Multiple areas of thrombosis, hemorrhagic infarction and ulceration in the esophagus—these lesions were limited to a circular band in the upper three-fourths of the lower one-third of the esophagus. They were approximately circular in outline and varied from 1 to 10 mm. in diameter. In the fresh specimen, minute areas of necrosis of the mucosa were visible over the infarcts, but there was no post-mortem digestion. Some of the lesions appeared recent with unbroken mucosa, while others seemed older, were brownish black and were the ones in which the minute areas of necrosis appeared. These lesions were essentially hemorrhagic erosions of the esophagus. Large region of atrophic red infarction (Zahn) of the liver; this requires no special description.

Gastric distention, as has been shown by Burton-Opitz[3] may produce complete obstruction of the gastric circulation. Working on dogs, it was found that air forced into the stomach squeezed the blood out of the vessels and flattened them, damming back the blood on

3. Burton-Opitz: Pflüger's Arch. f. d. ges. Physiol., 1908, cxxi, 150; also 1910, cxxxv, 205.

the arterial side. If considerable pressure (30 to 50 mm. Hg) were somewhat quickly applied, there resulted a sudden rise of venous pressure which was succeeded by a rapid fall, to rise again only when the intragastric pressure was relieved. An intragastric pressure of 50 mm. Hg was always sufficient to stop the flow of blood through the intramural vessels of the stomach. Increased intra-abdominal pressure, up to 70 mm. Hg, may likewise stop the portal circulation, which may be restored by removal of the pressure. The normal intragastric pressure in man varies from 6 to 9 and 20 to 162 cm. of water in the cardiac and pyloric ends of the stomach, respectively.

In the dog the normal intragastric pressures are approximately the same as those in man. Pressures may rise much above these figures in portions of intestine cephalad to a point of obstruction. Richards and Ruggles[4] fastened a recording apparatus in the intestine of a cat and found that the pressure in the obstructed region varied between 60 and 120 mm. Hg, and that when ergot and physostigmin were given, these figures were greatly exceeded—pressures amply sufficient to cause complete arrest of the circulation in the portion of bowel involved.

From the standpoint of pathological anatomy it is recognized that intestinal distention may lead to anemia of the bowel wall with stasis and thrombosis in the mesenteric blood vessels, leading occasionally to necrosis of the mucosa with the formation of so-called "dilatation ulcers."[5] The order in which this train of lesions develops is described as follows: intestinal distention, venous stasis, thrombosis, hemorrhage, necrosis, ulceration. The importance of the rôle of vasomotor paralysis and of the toxicity and infectiousness of the intestinal contents in the production of dilatation ulcers is uncertain.

Experimentally, where the presence of powerful toxins has been demonstrated not only in the intestinal contents, but also in the intestinal mucosa, submucous hemorrhages with ulceration occur frequently but not

4. Richards and Ruggles: See Cannon, Trans. Am. Gastro-Enterological Association.
5. Wilms: Der Ileus, Stuttgart, 1906, p. 56.

invariably.[6] When they do occur there is always an associated intestinal distention, thus making it appear that the latter is probably the important factor in their production.

In an obstructed gut, interference with the circulation probably develops as follows: The segment of bowel immediately cephalad to the obstruction is thrown into violent peristaltic contraction, thus increasing intra-intestinal pressure tremendously and squeezing most of the blood out of the intestinal capillaries. The peristaltic contractions increase in number and duration, in some cases developing into a tonic spasm of entire loops of gut. Gradually, exhaustion of the intestinal musculature thus devascularized makes its appearance and the gut slowly yields to the pressure of the contained secretions and gas, finally ballooning out to form, in the earlier stages, the areas of regional distention (known clinically as Von Wahl's sign) and later the general tympanites of ileus. As the increased intra-intestinal pressure from muscular contraction closed the intramural capillaries of the bowel in the first instance, so the pressure of the intestinal contents and the stretching and flattening of the capillaries in the distended gut tend to maintain that closure in the second. Thrombosis from stagnation is one of the results.

In the present case, conditions seem to have been about as follows: There was first marked increased intra-intestinal pressure. This caused collapse and occlusion of the thin-walled vessels in the intestinal wall with resulting stasis in the mesenteric vessels, in many of which thrombi presently formed. Meanwhile, with approximately the entire circulation through the small intestine shut off, the flow of blood through the portal vein became much reduced in volume and, as a result, the rate of flow through the fine venous radicles in the gastro-esophageal anastamosis — never very rapid, probably, under normal conditions — practically ceased and thrombosis from stagnation occurred. At

6. Stone, Bernheim and Whipple: Annals of Surgery, 1914, lix, 714.

the operation, the distention of the bowel was suddenly relieved; there was a sudden influx of blood into the portal system with almost explosive hemorrhagic infarction of the more extensively thrombosed areas in the intestines with occasional rupture of the mucosa and escape of blood into the bowel lumen, and the more gradual infiltration of the thrombosed areas in the esophagus. Simultaneously, many of the small thrombi in the mesenteric vessels were swept out into the portal vein and carried to the liver, there producing extensive infarction.

Hartwell and Huguet[7] and Gurd[8] have suggested, upon the basis of experimental work, that the powerful poisons described by Whipple and his associates in the contents and in the mucosa of closed intestinal loops, are the results of tissue autolysis. It is universally agreed that the prognosis in intestinal obstruction from any cause becomes doubly serious the moment that vascular injury develops. Tissue autolysis follows as a result of vascular injury. The manner in which increased intra-intestinal pressure may produce vascular injury has been discussed in the preceding paragraphs. Therefore, the suggestion that increased intra-intestinal pressure may be of primary importance in determining the onset of intoxication demands consideration. Experimentally, there seems to be no doubt but that loss of water is of extreme importance in producing the early symptoms of collapse in ileus and that, given sufficient water to replace that lost in the vomitus, urine, etc., a dog's life is not immediately imperiled. He suffers from starvation. His metabolism becomes that of a starving animal, unless vascular injury is produced, when the occurrence of death becomes but a matter of hours.

The complications or sequelae of intestinal obstruction appear to be intimately related to local vascular pathology. They are given by McGlannan[9] as follows: (1) toxemia; (2) gangrene; (3) peritonitis; (4) renal

7. Hartwell and Huguet: Jour. A. M. A., 1912, lix, 82. See also Hartwell, Jour. Exper. Med., 1913, xviii, 139.
8. Gurd: Jour. Infect. Dis., 1914, xv, 124.
9. McGlannan: Jour. A. M. A., 1913, lx, 733.

disturbances. To this list must be added a fifth complication named dehydration, the importance and probable cause of which has already been suggested, as has also that of toxemia. Renal disturbances are probably due to the above two factors. Gangrene as the result of vascular disturbance and peritonitis, developing through the escape of bacteria from intestines, the seat of injury from vascular disturbances, need but to be mentioned to be appreciated.

One of the common symptoms of ileus is paroxysmal cramp-like pain, which is commonly attributed to tension on mesenteric attachments. Might not this pain be produced in part by local tissue asphyxia, the result of vascular disturbances produced by the prolonged and violent contraction of the intestinal musculature, in other words, to the increased intra-intestinal pressure?

The evidence serves to emphasize anew the necessity for early operative interference in intestinal obstruction, of operation before extensive vascular changes have been induced. It suggests a reason why relief of the obstruction and drainage of the bowel, even in the absence of infection, fails to save a considerable proportion of cases—those cases in which thrombosis in the capillaries of the bowel wall and in the mesenteric veins prevents the efficient reestablishment of the circulation upon the removal of the intra-intestinal pressures. It also suggests caution against the too sudden relief of this pressure because of the danger, first, of embolism, and second, of acute explosive hemorrhagic infarction of portions of bowel in which the vascular apparatus might be able to accommodate a gradual return of the blood, but would be overwhelmed by its sudden influx, and third, of serious hemorrhage into the intestinal lumen from rupture of the mucosa over areas of explosive infarction.

The author is indebted to Dr. E. Wyllys Andrews for the clinical notes pertaining to the case reported in this paper.

Oct. 12, 1914.

BACTERIOLOGY OF CHOLECYSTITIS AND ITS PRODUCTION BY INJECTION OF STREPTOCOCCI

E. C. ROSENOW

The bacteriology of cholecystitis, as worked out heretofore, is largely the bacteriology of the contents and not the tissue of the gall-bladder wall. (The mechanism of infection of the gall-bladder and the production of gall-stones have not been fully worked out experimentally.) In a previous paper I pointed out that when streptococci, from various sources, attain a certain grade of virulence, they are prone to produce on intravenous injection cholecystitis and gall-stones, with large numbers of streptococci as the nuclei. In this connection the observations in the following case are of interest:

A woman, aged 62, with infected tonsils, high blood pressure, and a chronic arthritis, involving chiefly the small joints of the hands, contracted a "cold" and acute tonsillitis. Ten days later she developed a typical acute attack of cholecystitis. The symptoms continued for three weeks without jaundice. Then the pain shifted and the next day jaundice appeared, which deepened for a week and then gradually subsided. Jan. 19, 1914, five weeks after the beginning of the attack, an operation was made by Dr. Bevan. There was found a healing area, 1 by 1.5 cm., of necrosis at the fundus; but otherwise the gall-bladder was nearly normal.

The bladder was moderately distended with bile containing mucus and three soft "mulberry" cholesterin stones. Cultures from the bile were sterile; streptococci, colon bacilli and gas bacilli developed from the center of two of the stones, while from the emulsion of the excised piece of tissue only streptococci developed. The streptococci from both of these sources produced grayish-green, moist, non-hemolyzing colonies on blood agar and marked precipitation and acidity on dextrose-agar. They formed chains of diplococci and a large number of round cocci, which were often in masses, like some of the strains obtained from gastric ulcer. Sections from the wall of the gall-bladder, stained by Gram's method, showed a moderate number of streptococci.

Dog 57, of medium size, was injected intravenously, January 22, with the growth of the streptococcus from the wall of

the gall-bladder in 90 c.c. of ascites-dextrose broth, suspended in 7 c.c. of sodium chlorid solution.

January 24: Lame in the left hind leg. Fluid from knee-joint turbid. Cultures were made.

January 26: Cultures from knee-joints showed four green-producing, non-hemolyzing streptococci.

January 30: Found dead. Acute cholecystitis, enteritis, localized pancreatitis and nephritis. The wall of the gall-bladder was edematous, from 3 to 6 mm. thick; the mucous membrane was velvety, and covered in areas with a loosely adherent exudate; the cavity was distended with brownish fluid, containing masses of pus and mucus; pressure on the gall-bladder failed to discharge bile until the plug of the mucopus in the diverticulum was removed by passing a probe and by making firm pressure; a moderate number of dark concretions, of the consistency of putty, were found in the masses of mucopus in the gall-bladder and in the plug in the diverticulum. Smears from the crushed concretions, washed repeatedly in sodium chlorid solution, showed many streptococci. The liver was normal; there were whitish streaks in the medullary portion of the kidney, most numerous and largest near the pelvis, where a number of small ulcers were found; the cortex appeared normal; the urine contained leukocytes, some albumin and bile, and was highly acid; the mucous membrane of the lower end of the small intestine was hyperemic and covered with exudate in which were many streptococci; the fluid in the knee-joints was slightly turbid; the stomach, large intestine, adrenals, thyroid, lungs and heart were normal.

The bile, the plug of mucus and the wall of the gall-bladder yielded large numbers of streptococci. The joint fluids and the pelvis of the kidney gave a few colonies of non-hemolyzing streptococci. The blood remained sterile. Sections of the wall of the gall-bladder showed marked thickening and degeneration of the mucous membrane. Gram-Weigert stains show a large number of streptococci, especially in the submucosa.

The fluid contents of the gall-bladder, the center of stones, and particularly parts of the wall of the gall-bladder of twenty-nine cases of cholecystitis have now been studied according to my new method.[1]

1. Rosenow, E. C.: The Newer Bacteriology of Various Infections as Determined by Special Methods, The Journal A. M. A., Sept. 12, 1914, p. 903.

I wish here to express my very great appreciation for the opportunity afforded me recently at the Mayo Clinic where most of the cases occurred.

In five cases, the cultures from the wall were negative and in these the microscopic evidence of any changes was slight. In the remaining twenty-four cases, in all of which increase in thickness and other changes were more marked, streptococci were isolated in all but three and in pure culture in ten. In sixteen cases streptococci were found in the wall when the contents were sterile or contained only the colon bacillus. The colon bacillus was found with the streptococcus in only ten cases, once in pure form, once in association with the *Bacillus welchii,* and once with the staphylococcus. *Bacillus mucosus* was found in two cases of very acute cholecystitis. In two, diphtheroid bacilli were found and in one the fusiform bacillus was found. The fluid contents, usually bile, were examined in twenty-six cases: In twelve it was sterile; streptococci were found six times, colon bacilli nine times; staphylococcus three times; the *Bacillus mucosus* twice, and the fusiform bacillus once. The centers of gall-stones have been examined in thirty cases. Only two proved sterile; from the rest, streptococci were isolated in all but three, fourteen times in pure form and five times in association with the colon bacillus; the center of the stone, in one case, showed the typhoid bacillus in pure form while the center of two stones and the wall of the gall-bladder in a case with a clinical diagnosis of typhoid cholecystitis showed streptococcus in pure culture; in two cases the center of stones contained colon bacillus and the *Bacillus welchii,* and one the latter organism only; in some instances, streptococci were demonstrable in smear preparations from the center. Cultures from other portions of stones were usually sterile. The adjacent lymph-glands were examined in five cases. Streptococci were found in four, pure in three cases and in association with the *Bacillus welchii* in one case. In the cases in which a pure culture of the streptococcus was obtained from the tissue of the gall-bladder there seemed to be a definite relation

between the number of colonies which developed and the degree of change, especially if relatively recent inflammation was present.

A comparison of the results obtained from the bile, the stones and the wall of the bladder, in the individual cases, shows that a bacteriologic examination of the fluid contents gives trustworthy results only in the acute stage of the disease; during convalescence and in chronic cholecystitis the results are of little value and may be misleading. In chronic cholecystitis the bacteriology of the center of the stones is similar to that of the wall of the bladder.

The effect of the various organisms on intravenous injection has been tested in dogs and rabbits. All of the five strains of streptococci isolated from the wall of the bladder, one strain from an adjacent lymph-gland, and two out of five strains from the center of stones showed a marked affinity for the gall-bladder soon after isolation, and frequently produced no lesion elsewhere. Varying doses produced cholecystitis in nearly every animal injected. The severity of the lesions in the animals often corresponds to that found in the cases from which the strains are isolated. This affinity is soon lost, however, on cultivation as well as on animal passage. Five strains of colon bacilli, the one strain of typhoid bacillus, and one strain of the *Bacillus mucosus* in no instance showed any tendency to localize in the gall-bladder. It was not possible to produce cholecystitis with the streptococci by injecting them into the portal system, even with strains which produced cholecystitis practically every time when injected into the vein of the leg, and only localized cholecystitis developed at the point of puncture when the injection was made directly into the gall-bladder. In the animals which lived for a time, there was not infrequently observed the beginning formation of gall-stones containing numerous streptococci similar to the conditions found in several of the patients.

The strains of streptococci from the different cases show a striking similarity and resemble closely those from ulcers of the stomach. They produce either small, moist, grayish-brown or grayish-green, non-

adherent, non-hemolyzing colonies on blood-agar; they ferment mannite, lactose and salicin; they produce short chains in liquid mediums with clumps of cocci somewhat resembling staphylococci; they are of a rather low virulence, yet somewhat more virulent than strains from gastric ulcers, as manifested by their resistance to phagocytosis, by the smaller dose necessary to kill, and by the fact that, when cultivated for a time, they acquire affinity for the stomach and duodenum while the strains from ulcers, when passed through one or two animals, acquire affinity for the gall-bladder at the same time as they lose affinity for the stomach.

On animal passage, two of the strains produced both cholecystitis and pancreatitis, the lesions in the latter being most marked in the head of the pancreas.

The lesions most commonly observed other than cholecystitis, when these strains are injected especially in rabbits, are: ulcer of the stomach, hepatitis about the gall-bladder, myositis and myocarditis, arthritis, appendicitis and colitis.

The common presence of streptococci in the wall of the infected gall-bladder and in the center of gall-stones, often in pure culture, while absent from the bile and their affinity for the gall-bladder in animals, are strong evidence that streptococci are the cause of cholecystitis in man far more frequently than believed and serves to explain the good results reported by some as following cholecystectomy in cases of myocarditis, arthritis and other conditions.

Nov. 9, 1914.

THE QUANTITATIVE DETERMINATION OF BLOOD SUGAR, USING SMALL AMOUNTS OF BLOOD

S. STROUSE, I. F. STEIN AND ALAN WISELEY

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The study of blood sugar in the human being has been handicapped by the necessity of using large amounts of blood and by difficult technic. Within recent date several methods have been published

which aim to give accurate quantitive results on amounts of blood sufficiently small to allow repeated determinations in the same individual. Among these methods the one of Kowarsky offers the nearest comparison to standard chemical technic. The chemical methods on which this is founded are well known: (1) the precipitation of the albumin bodies of the blood by dialyzed iron, and (2) the Bertrand method of titration of sugar. Only 0.5 c.cm. blood is required for a test, and the percentage error of the technic with such small amounts of blood is lessened by the addition of a known amount of dextrose to the copper solution.

We have modified this method in slight technical details which will be published in full in a near number of *The Bulletin of the Johns Hopkins Hospital*, and have applied it to the study of a large number of normal as well as of pathological conditions. The first problem which required careful study was the significance of the variations of the so-called normal blood sugar. This problem we attacked by serial determinations on the same individual on the same day or succeedings days, and careful attention was paid especially to the diet factor. Our results showed conclusively that the "normal" blood sugar is represented by a curve which in an individual under ordinary conditions of living reaches its minimum before meals and its maximum shortly after meals. Thus the "normal" of a single person in one day may reach on the one hand 0.06 per cent. as a minimum, or 0.12 per cent., as a maximum, depending almost entirely on the carbohydrate content of the food. In a large series of determinations of the normal the mean figure of 0.084 per cent. obtained compares well with previously published studies made on much larger amounts of blood.

In pathological conditions the method also offers a scientifically accurate procedure, and in our hands has proved of diagnostic and therapeutic value in diabetes mellitus and other disturbances of carbohydrate metabolism.

CONCLUSIONS

1. The method of Kowarsky as modified is both scientifically accurate and simple.

2. The normal blood sugar is represented not by a fixed value, but by a curve which depends mainly on the carbohydrate intake for its variations.

Dec. 14, 1914.

PACHYMENINGITIS HEMORRHAGICA INTERNA

FLOYD B. RILEY

The hemorrhagic is the most common form of internal pachymeningitis. It has frequently been observed post mortem in adults, being an incidental finding in many bodies in which the principal causes of death were tuberculosis or heart and kidney diseases. It has also been found not infrequently in chronic alcoholism and in those diseases which are designated as hemorrhagic diatheses, as well as those which have a tendency toward brain atrophy, such as dementia paralytica, chorea chronica hereditaria and dementia senilis. According to Oppenheim,[1] it seldom has a syphilitic foundation. It does not seem to be so very rare among children, having been studied in recent years by Finkelstein,[2] Göppert[3] and others.

In 1913 Rosenberg[4] reported thirty-eight cases observed in four years in the Waisenhaus of Berlin. Holt[5] has seen several cases and Meigs reported two cases to the Chicago Pediatric Society in November, 1913.

The essential lesion is one of membrane formation on the inner side of the dura, and disseminated through this membrane are hemorrhages varying in size from minute to large collections. The color of

1. Oppenheim: Lehrbuch der Nervenkrankh., 5 Auflage, 2 S. 849-859, 1908.
2. Finkelstein: Lehrbuch der Sauglingskrankheiten I. Berlin, 1905.
3. Göppert: Drei Fälle von Pachymeningitis haemorrhagica mit hydrocephalus externus, Jahrb. f. Kinderheilk., Bd. 61, S. 51, 1905.
4. Rosenberg, O.: Ueber Pachymeningitis haemorrhagica interna, Berlin klin. Wchnschr., jg. 50, Nr. 49, S. 2272-2274, 1913.
5. Holt: Diseases of Infancy and Childhood, 1908, p. 751; Meigs, Grace L.: Jour. A. M. A., 1913, lxi, 2186.

the lesion varies from bright red in fresh hemorrhage to the darker pigmentations of old disintegrated corpuscles. The membrane may remain thin and delicate with very little color or it may become thick and tough, and sometimes lamellated owing to repeated hemorrhages superimposed one upon the other. It most frequently affects the convexity of the brain and is usually bilateral. It often leaves the posterior brain surface free and involves the base. Should the child recover or the condition persist for some time there may be encysting of the fluid portions to form hygromata or subdural cysts. Occasionally there may be calcification.

Although the conceptions of the pathological anatomy are fairly uniform there is considerable difference of opinion concerning the etiology. Virchow,[6] Heschel[7] and Melnikow-Raswedenkow[8] and a majority of pathologists hold the process to be a result of inflammation of the inner surface of the dura with formation of young connective tissue and young blood vessels with weak walls which rupture easily and produce hemorrhage. The other main view is that the hemorrhage is primary and the resulting lesion is an attempt at organization of the clot. This is the view held by most pediatricians. In France[9] the view is held that pachymeningitis hemorrhagica interna may be an incidental occurrence in the first stages of a developing lesion of which external hydrocephalus forms the second stage. In Germany[10] the main view has been that the nature of the lesion precluded the development of a hydrocephalus, and also that the primary condition was not one of inflammation but of hemorrhage through the walls of capillaries; hemorrhage following marked venous stasis.

6. Virchow: Verhandlung d. phys. med. Ges., Würzburg, Bd. 7, S. 129, 1856.
7. Heschel: Kompendium der allg. und spez. Path., 1855.
8. Melnikow-Raswedenkow: Zeigler's Beitrage, B. 28.
9. Leon d' Astros: Les Hydrocephalies, Paris, Steinheil, 1898.
10. Misch, Peter: Zwei Fälle von Pachymeningitis haemorrhagica interna, Jahrb. f. Kinderheilk., lxii, No. 12, S. 228; Jores and Laurent; Zur Histologie, etc., der Pachymeningitis, Ziegler's Beitr., xxix, 1901; Henoch: Berl. klin. Wchnschr., 1888, No. 29; Hahn, H.: Klinischer Beiträge zur Lehre von der Pachymeningitis haemorrhagica interna im frühen Kindesalter, Deutsch. med. Wchnschr., xxxvii, S. 1518, 1911.

Göppert's[11] three cases, however, were associated with external hydrocephalus.

Birth trauma is regarded by Doehle[12] as a possible factor.

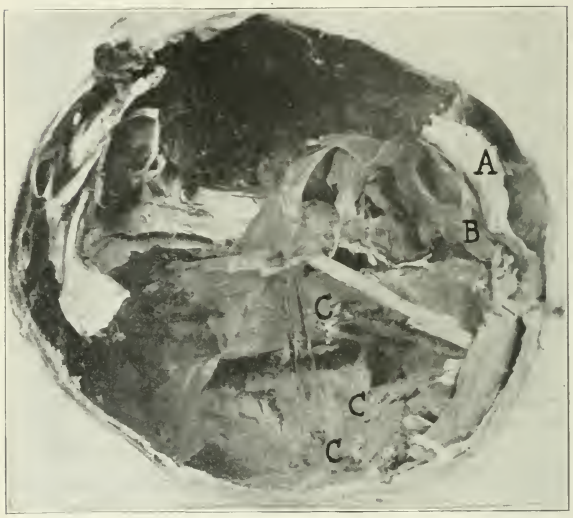
Trauma and convulsions are mentioned by Schindler[13] and Hutinel. Scurvy is given by Sutherland[14] as a predisposing cause. Syphilis as a very important etiological factor is emphasized by Doehle,[15] Heubner,[16] Weyke[17] and Leon d'Astros.[18]

Rosenberg concludes that the lesion does not have an inflammatory origin. He believes that there is weakness or disease of the capillaries of the dura mater and as a result of venous stasis in the sinus cavernosus and its tributaries, hemorrhage occurs. He cites two facts, viz., first, that the process is on the inner surface of the dura and second, that it is usually accompanied by transudation, as support for the primary hemorrhage idea. Eighty per cent. of the thirty-eight cases studied by him had a bloody rhinitis previously and in half of these diphtheria bacilli were found. He considers the finding of this lesion in luetic cases as much a part of the luetic picture as are those nasal symptoms recognized as characteristic for syphilis.

The specimen I have to show (Fig. 1) is from a case that occurred in the service of Dr. Walker in the Children's Memorial Hospital. I am indebted to him for the privilege of showing the specimen and to Dr. Meigs who reported it to the Pediatric Society. The child was 4 months old. It was brought to the hospital because of failure to gain, vomiting and constipation. It was small, emaciated and old looking with a large head and a small face. The anterior

11. Göppert: Drei Fälle von Pachymeningitis haemorrhagica mit Hydrocephalus externus, Jahrb. f. Kinderh., Bd. 61, S. 51, 1905.
12. Doehle: Ueber chron. Pachymeningitis, Berlin Int. Kongress, xvii, S. 40, 1890.
13. Schindler, Rudolph: Ein Fall von Meningocele spuria traumatica mit pachymeningitis haemorrhagica interna, Jahrb. f. Kinderheilk., 76, S. 160-179, 1912; Hutinel: Hemorrhagies Meningees, Pediatr. Pract., Jg. 11, Nr. 9.
14. Sutherland: Brain, 1904.
15. Doehle: Ueber Chron. Pachymeningitis, Berl. Int. Kongress, xvii, S. 40, 1890.
16. Heubner: Eulenberg's Realenzyklopadie.
17. Weyke: Dissert. Kiel, 1889.
18. Leon d'Astros: Les Hydrocephalies.

fontanelle was four fingers in width and the coronal suture very wide. Circumference of head was 41.25 cm. upon admission and 39 cm. after numerous lumbar punctures performed during twenty-four days. The general examination except for enlarged spleen and lymph glands and emaciation was negative. Urine was negative. The neck was not rigid. Lumbar puncture at first gave a clear fluid under increased



Specimen of pachymeningitis hemorrhagica interna showing interior of skull cap with dura and membrane. A. Dura separated from skull. B. Membrane of internal pachymeningitis stripped from the under surface of the dura. C. Cavity beneath fontanelle puncture in which reddish fluid had collected.

pressure. Fontanelle puncture gave a bloody fluid. Clinical diagnosis of decomposition and internal hydrocephalus was made. Post mortem was made thirty-six hours after death and examination of the head only was permitted. When skull cap was removed bloody fluid escaped. Between the dura and brain over vertex and base was a hemorrhagic exudate with

membrane formation, adhering to the under surface of the dura. This membrane could be easily stripped away. In one place beneath the fontanelle puncture about one-half ounce of reddish fluid had collected.

The histological preparation showed thickening of the dura mater with capillaries radiating at right angles into a new membrane rich in capillaries and hemorrhage.

Children's Memorial Hospital.

Dec. 14, 1914.

SUBMUCOUS FIBROMA OF THE STOMACH CAUSING PERFORATION OF THE MUCOSA AND PYLORIC OBSTRUCTION

WILTON McCARTHY AND LUDVIG HEKTOEN

The patient, from whom the specimen was removed, was a woman, age 40, who consulted Dr. A. H. Leonard of Mitchellville, Ia., on April 3, 1914, because of headache, chilly sensations, and distress in the stomach. For some time before she had complained of constipation and epigastric distress relieved somewhat by belching. April 5 she went to bed suffering from increased pain in the epigastrium and vomiting, which continued, the temperature rising to 103. No food was taken. The general condition became less favorable, the vomited matter darker in color. On April 8 Dr. Wilton McCarthy made a pylorectomy. Peritonitis was then present. Death two days later.

The specimen preserved in formalin may be described summarily as follows: It consists of a part of the stomach adjacent to the pylorus, irregularly oval in outline when spread out, 18 cm. in the longest diameter and 14 cm. transversely at the center, with an irregularly cylindrical, fibrous tumor, 12 cm. long and approximately 5 cm. in transverse diameter, situated loosely in the submucosa, the long axis being parallel with the long axis of the stomach. The half of the tumor near the pylorus is covered by the mucosa and bulges toward the cavity of the stomach, its periphery being marked by a deep semicircular sulcus which is 4 cm. inside the pyloric ring at the nearest point. Approximately at the center of the bulge is a flattened circular nodule, 6 cm. in

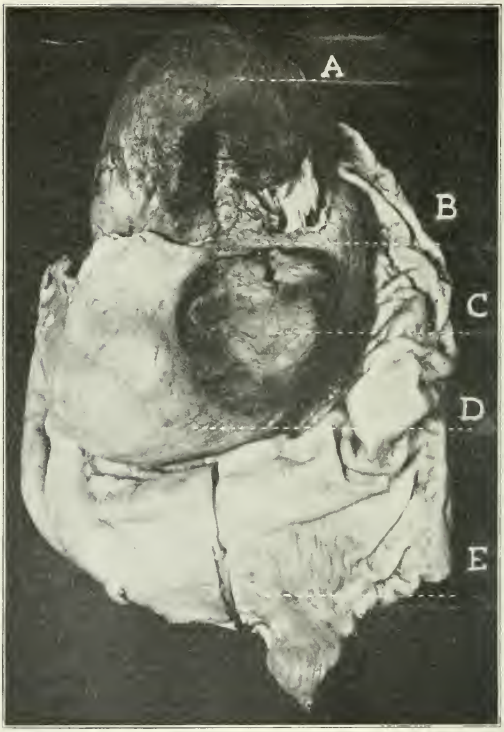


Fig. 1.—A. Free end of tumor. B. Margin of mucosa. C. Button-like node projecting through mucosa. D. Tumor in submucosa. E. Pylorus.

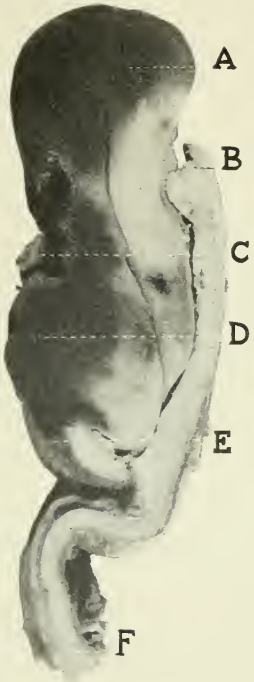


Fig. 2.—A. End of tumor. B. Margin of muscular coat. C. Margin of defect in mucosa. D. Congested node engaged in hole in mucosa. E. Margin of defect in mucosa. F. Pylorus.

diameter, which projects through a defect in the mucosa in which it is held very much like a button by the button-hole. It can be buttoned and unbuttoned, so to speak, and its substance is red from congestion caused apparently by the constriction of the margins of the defect in the mucosa (the button-hole). Its surface is necrotic. The end of the tumor farthest from the pylorus projects several centimeters from the cut edges of the wall of the stomach and gives the impression because of congestion and a line of compression of having been constricted by a mechanism similar to that just described, but it is impossible to speak definitely on this point because the part of the stomach in question is not accessible for examination (Fig. 1).

On bisecting the specimen in its long diameter (Fig. 2) the appearances it has been attempted to describe become intelligible; one sees the tumor loosely situated in the submucosa, the sulcus near the pylorus, the congested button-like nodule in the grasp of the margins of the defect of the mucosa, and the congested and apparently compressed globular, free end of the tumor. On the cut surface the tumor appears firm and fibrous, but deeply congested in the districts that appear black on the photographs. The tumor is easily shelled out of its bed, being firmly connected with the wall of the stomach at one small point only, namely, to one side of the end near the pylorus. The muscular coat of the stomach appears somewhat hypertrophied; its serous surface is rough as if from torn fibrous adhesion.

Microscopically the structure of the tumor is that of a typical fibroma.

We have then a specimen of a submucous fibroma of the stomach near the pylorus, irregularly cylindrical in shape, which caused circumscribed perforation of the mucosa by pressure and also obstruction to the pylorus.

Dec. 14, 1914.

THE RELATION OF HYDROCHLORIC ACID TO THE MORPHOLOGICAL CHANGES INDUCED BY CHLOROFORM

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Central lobular liver necrosis of the type found in "late chloroform poisoning" has been produced experimentally by other aliphatic halogen substituted com-

pounds, viz., CH_2Cl_2, CCl_4, $CHBr_3$, CHI_3, C_2H_5Cl, C_2H_5Br, C_2H_5I, $C_2H_4Br_2$. It could not be produced with ether or chloral hydrate. Chloroform in vitro is decomposed by oxygen into HCl and $COCl_2$. The latter is further changed by water into 2HCl and CO_2. Analogous decompositions occur with the other drugs named. The necrosis, and perhaps also the edema, hemorrhages and fat infiltration which accompany it, are held to depend mainly on the action of the respective halogen acids formed in the breakdown of these substances in the body.

1. Oral or intra-portal administration of HCl, in suitable concentrations, produces liver necrosis, edema, hemorrhages and fat accumulation.

2. In chloroform poisoning central necrotic areas in the liver show a higher H^+ and Cl^- content than control normal livers when the H^+ content is determined by neutral red and naphthol blue, and the Cl^- content by $AgNO_3$.

3. The formation of the respective halogen acid after the administration of each of the drugs above mentioned is shown by the occurrence of the neutral salts of these acids in the urine.

4. Alkali given in proper concentration inhibits the production of the necrosis and other changes by chloroform.

5. The powers of CCl_4, $CHCl_3$ and CH_2Cl_2 to produce these changes are directly proportional to the amounts of HCl which they may yield by decomposition, and the changes they are shown by these drugs in the order mentioned.

6. Of the ethyl compounds the chlorid is least powerful in this respect and the iodid the most powerful. This agrees with their respective ability to form HCl, HBr and HI outside of the body.

7. The failure to produce the same type of changes with chloral hydrate agrees with its failure to form an appreciable amount of HCl in its breakdown in the body.

Dec. 14, 1914.

LOCAL INFECTIONS DUE TO INTRAVASCULAR DISSEMINATION OF BACTERIA: THE ASSOCIATION OF DIPHTHEROID BACILLI WITH VARIOUS DISEASE CONDITIONS *

E. C. ROSENOW

(From the Memorial Institute for Infectious Diseases, Chicago.)

In this paper I wish to record certain results which indicate that the embolic origin of infection is far more common than has been believed in the past, and that a certain type of thrombosis is apparently due to a particular diplococcus. I wish also to relate results of cultures from the blood and other tissues together with illustrative cases which indicate that diphtheroid bacilli may be the cause of certain unusual forms of infection.

The hematogenous origin of infection in regions which do not normally harbor bacteria, such as the endocardium, pericardium, joints and bone is accepted. The mode of origin of appendicitis, ulcer of the stomach, cholecystitis and other infections in regions normally harboring bacteria is not so clear and is usually considered a local invasion even where the clinical facts suggest an hematogenous origin. Until recently this view was accepted because of the meager experimental evidence that these conditions may be produced by intravenous injection. In some experiments which I have performed recently the importance of the blood stream as a carrier of infection is very evident and the elective localization of streptococci from appendicitis, ulcer of the stomach, cholecystitis and rheumatic fever in the corresponding organs of experimental animals occurs commonly with the strains soon after isolation while later this affinity is lost. The details of the results of these experiments are reserved for other papers.

By the application of improved methods it has been learned that the blood stream is invaded during life

* Presented at a joint meeting of the Chicago Surgical and Chicago Pathological Societies, Jan. 8, 1915.

by bacteria far more frequently than has been known in the past. The mechanism of the entry of bacteria into the blood stream is not always clear. The importance of large thrombi in this connection, however, is evident. The common occurrence of typical septic temperature in cases of sinus thrombosis, for example, where the bacteria grow in the thrombus and intermittently invade the blood, suggests that a similar mechanism causes puerperal sepsis or the septic fever which sometimes follows appendectomy, for example, where there is no evidence of gross thrombosis or abscess formation. In some instances there seems to be an adaptation which allows the micro-organism to enter and grow in the circulation where little or no local disturbance exists.

The important rôle of infection as the cause of thrombophlebitis is very evident clinically and anatomically in those cases where there is softening of the thrombus and suppuration in the region where emboli lodge. Here bacteria of a relatively high grade of virulence are responsible. The cause of the formation of postoperative thrombi following herniotomy or appendectomy, for example, where they form in other regions than the field of operation, producing little fever or other symptoms, but giving rise commonly to fatal pulmonary embolism is not so clear. I have had opportunity to make cultures from the blood or thrombus or both in a number of these cases. A pure culture of a Gram-positive, relatively avirulent, short chained, non-encapsulated, green producing diplococcus has been isolated from one case of primary portal thrombosis, from four cases of fatal postoperative pulmonary embolism, following appendectomy, herniotomy and hysterectomy, from the blood in two cases of thrombosis following labor (both of which recovered) and from the blood in one case of quite generalized venous thrombosis which began in the iliac veins in a case of sarcoma of the pelvis with marked pressure. The same organism was isolated in almost pure culture from the thrombus in the pulmonary artery which caused the death of a patient following a postoperative peritonitis. The

cultures from the peritoneal exudate showed mostly hemolytic streptococci, but also a few of the above green producing diplococci.

Intravenous injection of the strain from the case of portal thrombosis produced thrombosis in the portal vein in rabbits. It seems therefore that cases of thrombosis in which there is little or no fever, which occur commonly a week or ten days after anesthesia or operation, the time when the blood coagulates rapidly as shown by Hamburger and Ewing[1] are associated commonly with a particular organism. The fact that the thrombus forms often in regions other than the place of trauma and in cases where no apparent infection exists emphasizes the importance of searching for and removing, if possible, foci of infection which are known to harbor similar organisms such as the tonsils and pus pockets about the teeth, a point not yet sufficiently recognized. The etiologic rôle of the organism can scarcely be questioned, but apparently it can produce thrombosis only when the coagulability of the blood is high and when a certain amount of stasis exists.

The exact relation of diphtheroid bacilli to disease in man is not well understood, largely because when injected into animals they frequently show little or no pathogenic powers. That they produce disease, however, in some instances is certain, because Ghon and others have demonstrated them in the vegetations of certain cases of endocarditis and I have shown their presence in the blood and the nodes of erythema nodosum and have produced similar lesions in animals by intravenous injection.

Blood cultures made by the usual technic rarely yield these organisms. By means of a method,[2] however, in which due regard is paid to the question of oxygen pressure, I have succeeded in isolating organisms of this type in pure culture from the blood during life in two cases of erythema nodosum, two cases of exophthalmic goiter, in four cases of Hodgkin's disease during the febrile period, in two cases of endo-

1. Jour. Am. Med. Assn., 1908, li, 572.
2. Rosenow: Jour. Am. Med. Assn., lxiii, 1914, 903.

carditis, in one case of rheumatism and in two peculiar fatal cases of purpura hemorrhagica. The two cases of purpura had similar histories. Pericarditis was present in both, marked hemorrhages of the skin and mucous membranes occurred, the fever was never high, leukocytosis was slight or absent, but there was marked mental and cardiac disturbance from the beginning. Both had some disturbance of the teeth previously, and in one the same organism as was found in the blood was isolated from a suppurating sinus at the root of an abscessed tooth.

The results in the following case are of interest: A girl, aged 14 years, a case of Dr. Miller, had a bronchopneumonia following a severe cold from which she apparently recovered, but April 14, 1914, five days previous to making the blood culture, there was discovered a mitral murmur associated with return of some fever. The day after making the blood culture she developed arthritis, but ultimately made a complete recovery. The blood culture showed a pure growth of a diphtheroid-like bacillus which produced, when injected into a rabbit, marked hemorrhages in the lungs and bronchopneumonia, a multiple non-suppurative arthritis, endocarditis, pericarditis, myocarditis and a localized infection in the muscular coat of the stomach.

A diphtheroid bacillus was found in the abscess of a tooth, in the blood, in the erythematous node of the skin of the forearm during life and in the vegetation and acute ulcers of the stomach in a case of acute fatal arthritis following extraction of abscessed teeth in a patient of Dr. Billings. The abscesses may have been the source of infection of the chronic arthritis which was present for some years previously.

The findings in a man 27 years of age, a patient of Dr. Whitaker, are of interest. For the past two years he has had occasional disturbances of stomach accompanied by pain. Six months ago had an attack of dull aching pain in the epigastric region which was continuous and accompanied by nausea and constipation and relieved by sitting down or lying on his

back and temporarily by taking food. This attack lasted seven days and then disappeared. An exactly similar attack occurred ten days before he was given, in the late forenoon of October 26, osteopathic manipulations of the abdomen. Three hours later he was seized with a violent pain in the epigastrium which doubled him up, the abdomen became tense, the temperature was subnormal, the pulse rapid and irregular, there was marked pallor. A diagnosis of perforated duodenal ulcer was verified the same night at operation by Dr. Whitaker. A large accumulation of pus had already taken place, the small perforation in the indurated ulcer (2 by 1.5 cm.) on the anterior surface of the first portion of the duodenum was closed and drainage established. Ten days later the patient developed an annoying dysentery, but this disappeared in a week. The symptoms referable to the ulcer gradually subsided, but he developed a typical septic fever accompanied by marked and exhausting sweats, weakness and emaciation, which gradually grew worse. After some weeks of septic fever the patient developed severe pain in the middle portion of the femur and circumscribed red, tender, symmetrically-placed nodules along the course of the subcutaneous veins in the forearm.

On December 18 Dr. McArthur saw the patient and suggested having a blood culture made to determine the cause of the sepsis, since examination of the abdomen was quite negative. The pus which I expressed from the tonsil yielded a predominating and large number of diphtheria-like bacilli together with some streptococci, while the blood yielded a pure growth of a similar bacillus. A vaccine prepared from the diphtheroid bacillus obtained from both regions was followed by a disappearance of the septic fever and the pain in the femur, the nodules on the forearm disappeared, the appetite returned and he made an uninterrupted recovery.

From a consideration of these findings the idea that a similar variation in the pathogenic powers of the diphtheroid group of organisms exists as in the streptococcus group, receives some support; however, the

possibility that the diphtheroid bacilli are mere secondary invaders must be considered seriously until definite experimental proof has been brought forward that they are actually the cause of each individual disease.

Jan. 8, 1915.

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ON THE SPECIFICITY OF PLACENTAL PROTEINS IN SKIN REACTIONS OF THE HUMAN BODY

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AND

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It seemed to us that if a ferment were circulating in the blood of pregnant women the principle upon which the Abderhalden test depends, then by introducing some of this protein under the skin a reaction might be obtained which would differ in nature or intensity from the reaction obtained in non-pregnant women.

To detect differences in the reaction of pregnant and non-pregnant cases the following points were observed:

1. Local reaction as manifested by size, redness, tenderness and painfulness, and by the involvement of the regional lymphatics.

2. General reaction, as shown by changes in the temperature, pulse, and also by headache, malaise, backache, chilliness, itching, nausea and vomiting, and uterine contractions in the cases of pregnancy.

3. Other special symptoms of anaphylactic reaction such as respiratory disturbances, changes in blood pressure, eosinophilia, and changes in the urine.

We used protein fractions of the placenta as well as whole placenta. These fractions were obtained by extracting fresh placental tissue, blood free with water

normal salt, and 0.3 per cent. HCl. A glycerin emulsion was used for the von Pirquet scarification. The proteins were introduced by the von Pirquet, subcutaneous, and intracutaneous methods. The first two methods gave such unreliable results that they were soon discarded in favor of the third method. Great care was taken to inject equal amounts at equal depths in the skin.

The pregnancy cases were all healthy women, and almost all primiparae in the last two months of pregnancy. The control cases were normal women of about the same age.

RESULTS AND CONCLUSIONS

The results were not uniform. Positive reactions were obtained in both non-pregnant and pregnant cases. Some of the non-pregnant cases reacted more strongly than some of the pregnant cases. On the whole, we are inclined to think that there was a slight balance in favor of the pregnant cases; but nothing of sufficient intensity to give it diagnostic value. The general reaction was conspicuous by its absence. We could detect none of the symptoms of anaphylactic reaction as reported by other authors who used other proteins in animals and occasionally in man.

This speaks against the theory that the pregnant woman is specifically sensitized to placental proteins. The lack of a general anaphylactic reaction also speaks against the view that the pregnant woman is in fact a sensitized woman.

We realize that the methods of preparation of the proteins is open to the objection that our manipulations may have so changed the substrate that the specific ferments could no longer attack it and break it down. That may be true, and yet other proteins capable of sensitizing and producing anaphylactic shock can be handled in a similar manner and retain their specificity, as shown by Vaughn, Wells and others.

Nov. 9, 1914.

A STUDY OF FAT EMBOLISM ASSOCIATED WITH FRACTURES

E. R. LeCOUNT AND HARRY GAUSS
(From the Pathological Laboratory of Rush Medical College, Chicago.)

The examinations this report concerns were undertaken because of the general failure to attach little or no clinical importance to fat embolism, of the common tendency to ascribe the delirium following fractures to the use of alcohol and finally because we desired to ascertain whether the amount of fat as demonstrable by ordinary laboratory methods was in any way related to the severity of the symptoms.

In only one of the fourteen cases of fat embolism studied was a clinical diagnosis of fat embolism made. This patient, a locomotive fireman, sustained a fracture of both bones of one leg in a railroad accident, was admitted to the Presbyterian Hospital to the service of Dr. Graham. On the second day he developed the pulmonary, cerebral and cardiac symptoms of fat embolism and punctate hemorrhages appeared in the skin. The patient was seen by most of the surgeons and by various physicians of the hospital staff and their diagnosis was confirmed by the post mortem examination. He died on the fourth day.[1]

Microscopic examination of the organs was made in the following manner:[2]

The tissues were fixed in a 10 per cent. formalin solution, infiltrated for two hours in a 10 per cent. gelatin solution at 37 C., hardened in formaldehyd vapor at 37 C. for 24 to 72 hours, sectioned and stained with osmic acid and sudan III. Sections were also studied after paraffin or celloidin infiltration and staining methods commonly used to bring out histological details. Fifty sections were examined from each piece of tissue and of these, five sections containing average

1. The various observations regarding this death from fat embolism were reported to the Illinois Medical Society, March 23, 1910, by Dr. Evarts A. Graham, but so far as we know, they have not been published.
2. A slight modification of the method suggested by Bolton and Smith, Centralbl. f. allg. Path. u. path. Anat., 1903, xiv, 620.

amounts of fat emboli were set aside for comparison. When the sections were collected, they were carefully gone over and the amount of fat in ten fields of each organ was compared with the amount in ten fields of the same organ of Dr. Graham's patient, which, because of the pronounced clinical manifestations and anatomic changes, was taken as a standard; the ratio

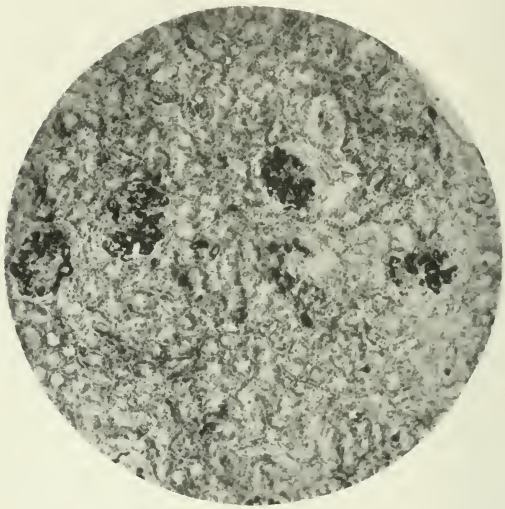

Fig. 1.—Fat in the renal glomeruli assumed as 100 per cent. Case 1. 60x.

was taken as percentage. Then the percentages of the several organs were averaged, the results being that quantities of fat emboli ranging from 5 to 45 per cent. were found in the organs removed from the bodies of thirteen persons dying with fractured bones. For uniformity of results, only the heart, lungs, kidney and liver sections were used for computation, although other organs were also examined.

In all instances, the lung tissue where examined contained fat emboli, which ranged in size from 5 to 225 μ in diameter; also there was active hyperemia in all, and microscopic hemorrhages in half. In all but one, the heart muscle contained vessels with fat emboli in them from 5 to 40 μ in diameter; also there was hyperemia, hemorrhages in twelve, and fatty degeneration in six. The kidneys from all fourteen bodies

TABLE 1.—ANATOMIC CHANGES

Case No.	Quant. Estim. Compared to No. 1	Lung			Heart					Kidney				Liver		
		Size of Fat Emboli, microns	Act. Hyperemia	Hemorrhages	Size of Fat Emboli, microns	Act. Hyperemia	Hemorrhages	Fragmentation	Fatty Degen.	Size of Fat Emboli, microns	Act. Hyperemia	Hemorrhages	Fatty Degen.	Size of Fat Emboli, microns	Fatty Infilt.	Engorgement
1	100%	10- 50	+	+	10-40	+	+	—	+	20-80	+	+	—	20-30	—	+
2	35%	15- 35	+	+	*	+	.	.	.	10-75	+	+	—	5-10	+	+
3	35%	15- 60	+	+	—	+	+	—	—	5-35	+	+	+	30-50	+	—
4	35%	15- 60	+	+	10-15	+	+	+	—	15-40	+	—	+	5-15	+	+
5	45%	20-225	+	—	20-30	+	+	—	+	20-60	+	—	+	—	+	—
6	40%	10- 90	+	—	5-15	+	+	+	—	10-30	+	+	+	—	+	+
7	10%	10- 35	+	+	*	.	.	.	.	5-40	+	—	+	*	.	.
8	15%	10- 25	+	—	5-20	+	+	—	—	5-40	+	+	+	—	++	+
9	25%	10- 35	+	—	5-15	+	+	+	—	10-60	+	—	+	10-15	++	+
10	25%	*	.	.	5-15	+	+	—	+	10-60	+	+	+	10-15	++	+
11	20%	5- 80	+	—	10-20	+	+	+	+	5-60	+	+	+	—	++	+
12	10%	20-100	+	+	10-20	+	—	—	+	40-60	+	+	—	—	++	+
13	25%	10- 60	+	—	15-35	+	+	—	+	15-55	+	+	+	—	++	+
14	5%	15- 50	+	—	*	.	.	.	.	10-45	+	+	++	—	++	+

Cerebral fat emboli in 1, 3, 4, 11. (Others not examined microscopically.)

Edema of the brain in 1, 2, 3, 5, 8, 11, 14.

Fat droplets in the blood in 1, 6, 7, 8, 9, 11.

Petechial hemorrhages in the skin or organs in 1, 4, 6, 7, 8, 10, 11, 12, 13.

* Not examined.

contained fat emboli from 5 to 80 μ in diameter, and there was hyperemia in all, hemorrhages in ten, and fatty degeneration in thirteen. In the liver of six bodies, emboli were found, from 5 to 30 μ in diameter; in twelve there was engorgement of the vessels and fatty infiltration. In seven this accumulation of fat in the liver cells was marked, covering one-half to seven-eighths of the microscopic fields.

Fat emboli were also found in the brain, suprarenal glands, gastric mucosa, testis, and spleen in several instances. Edema of the brain was diagnosed grossly in seven, and fat droplets[3] were detected in the blood at the time of the post mortem examination in seven. In this connection, it may be stated that the fat was present in considerable quantities, sufficient to attract

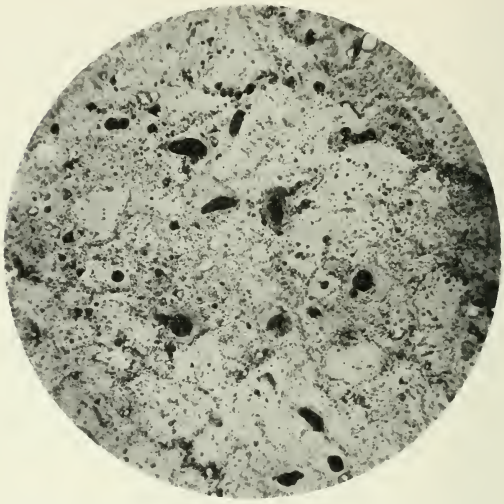

Fig. 2.—Lung with an abundance of fat emboli reckoned as 100 per cent. Case 1., 60x.

attention when the blood flowed from surfaces made by sectioning the organs. Petechial hemorrhages were found in the skin or organs of nine bodies, and fat was found in urine from the bladder once.

3. Fat droplets are easily seen by the unaided eye, if the blood is held in the sunlight. Another method used, and one easily carried out, is to examine microscopically the top layer of fluid pipetted off from a tall glass tube filled with blood taken from the heart and kept erect in the cold over night.

In contrast with the diversity of conditions presented in Table 1, the clinical symptoms (Table 2) were quite uniform. All the patients after a variable period of consciousness passed into a stage of restlessness, and in twelve this took on the form of delirium, and restraint was needed for eleven, and a similar number passed from their delirum into coma. All developed marked dyspnea; in a few, râles were heard; in all, the respiratory rate was increased, with

TABLE 2.—CLINICAL OBSERVATIONS

Case No.	Sex and Age	No. Days Patient Lived	Bone Fractured	Temp.		Symptoms												
						Cerebral				Resp.			Cardiac					
				Lowest	Highest	Restlessness	Delirium	Restrained	Coma	Dyspnea	Râles	Rate	Other Symptoms	Weak Pulse	Cyanosis	Rate		Urine and Feces Involuntarily
1	M. 35	4	Tib. fib.	97.8	106.2	+	—	—	+	+	+	64	C-S	+	+	164		+
2	M. 64	5	Humerus	98.0	105.4	+	—	—	+	+	—	60	A-H	+	—	120		+
3	M. 52	5	Pelvis	98.8	105.0	+	+	+	+	+	—	44	Co	+	+	130		+
4	M. 59	3	Humerus	?	?	+	+	+	—	+	—	?	A-H	+	—	142		—
5	M. 42	6	Tib. fib.	97.0	103.0	+	+	+	+	+	—	40	.....	+	—	150		+
6	M. 52	3	Humerus	98.0	104.2	+	+	—	—	+	—	30	.....	+	—	128		+
7	M. 45	5	Femur	98.4	107.4	+	+	+	+	+	—	42	A-H	+	+	140		+
8	M. 51	6	Tib. fib.	98.0	105.6	+	+	+	+	+	+	68	A-H	+	—	120		+
9	M. 58	14	Femur	98.0	104.0	+	+	—	+	+	+	60	Co	+	—	136		+
10	M. 62	2	Femur	101.0	106.0	+	+	+	+	+	+	72	.....	+	+	134		+
11	M. 56	6	Tib. fib.	98.0	106.0	+	+	+	+	+	—	60	C-S	+	—	156		+
12	F. 35	7	Tib. fib.	98.6	105.2	+	+	+	—	+	—	34	.....	+	—	140		—
13	M. 39	5	Calcaneus	99.6	108.2	+	+	+	+	+	—	60	.....	+	—	140		+
14	F. 90	17	Femur	96.9	101.4	+	+	+	+	+	—	48	.....	+	—	112		+

Diagnosis of delirium tremens in 4, 6, 8, 12.
Diagnosis of delirium tremens and lobar pneumonia in 7, 10.
Diagnosis of delirium tremens and hypostatic pneumonia in 9, 11.
C-S=Cheyne-Stokes, A-H=air hunger, Co=cough.

an average of 53; in all, the pulse became rapid, weak and shallow, averaging 137. Urine and feces were passed involuntarily in twelve and in the other two, the records are incomplete. All of the patients were admitted with a temperature normal or slightly subnormal, except one; and in all, the temperature rose steadily to the time of death, with an average of 105.2 F. at the time of death. The bones fractured were generally the long bones, the femur in four of the

patients, the humerus in three, the tibia and fibula in five, the calcaneus in one and the pelvis also in one. The average age of the patients was 53 years, and the average time that they lived after the injury, six days.

As stated, fat embolism was not diagnosed clinically except in the first instance. Four of the clinical diagnoses were "fracture," four others "fracture compli-

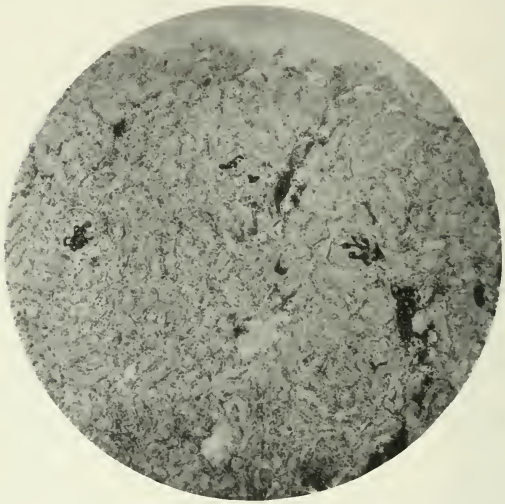

Fig. 3.—Fat emboli in the kidney estimated as 40 per cent. as abundant as shown in Fig. 1, dia. 60.

cated by delirium tremens," two as "fractures complicated by delirium tremens and lobar pneumonia," two others as "fracture complicated by delirium tremens and hypostatic pneumonia," and "cerebral hemorrhage" once. Regarding these diagnoses of pneumonia, only once was it in a measure confirmed by finding a slight hypostatic bronchopneumonia at the post mortem examination. As for the diagnosis of

delirium tremens made eight times, it has seemed to us, in view of the changes in the brain and the amount of fat in the blood vessels, that the use of alcohol may not have been altogether responsible for the delirium, or to state it in another way, fat embolism as a cause of delirum following fractures and so commonly diagnosed as delirium tremens has not been given the con-

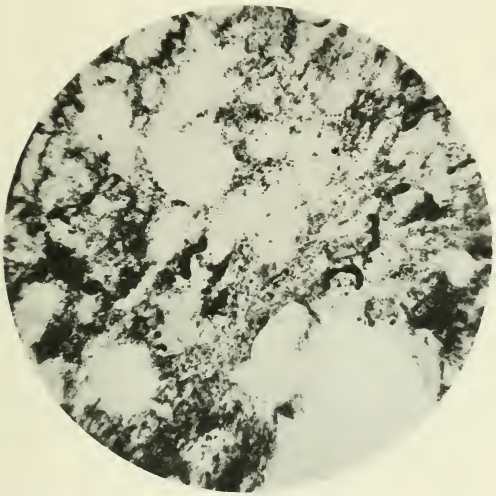

Fig. 4.—Forty per cent. of fat embolism in the lung as compared with conditions illustrated by Fig. 2, dia. 60.

sideration it deserves. For a number of these thirteen patients[4] a history of alcoholism was not obtained.

We obtained no evidence that the amount of fat in the blood vessels at the time of death demonstrable by such methods as we employed was in any way pro-

4. The thirteen individuals died in the Cook County Hospital and the post mortem examinations were a part of the inquiry conducted by the coroner of Cook County or his deputies.

portionate to the severity of the symptoms; on the contrary, the evidence at hand indicates that the amount of fat in the blood as emboli in persons with fractured bones varies from time to time; indeed, there is still opportunity for investigation to prove that death with fractured bones and without such complications as pneumonia or infection is not caused by fat

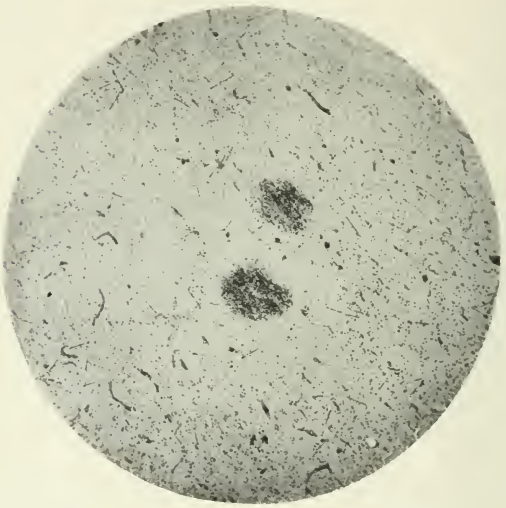

Fig. 5.—Section of brain with small hemorrhages due to fat emboli, 60x.

embolism, even though but little fat can be found as emboli in the blood vessels at the time of death.

Finally, we wish to emphasize the medicolegal importance of fat embolism and the difficulty in maintaining in civil or criminal suits that deaths accompanied by conditions such as those discussed here were due solely to delirium tremens.

Nov. 9, 1915.

FOUR EXAMPLES OF THROMBOSIS PRIMARY IN THE PORTAL VEIN

GEORGE S. MATHERS
(From the Pathological Laboratory of Cook County Hospital.)

There are a number of comprehensive articles on this subject, and especially noteworthy for their review of the literature are those of Brown,[1] Herringham,[2] Rolleston,[3] Lissauer,[4] and Lewis and Rosenow.[5]

The disease is not common. Lissauer found only sixty-eight examples of thrombosis of the portal vein or its tributaries in the records of 26,687 autopsies at the University of Breslau and Lewis and Rosenow in 1909 were able to find only 20 instances of primary portal thrombosis in the literature. It is usually associated with some inflammatory or malignant disease of the adjacent abdominal viscera. The primary causes are the same as for thrombosis elsewhere and is usually infective in origin. The causative organisms most commonly found are streptococci and staphylococci of low virulence.

The wall of the vein is invaded by bacteria which give rise to infiltration, endophlebitis and thrombosis. The lumen of the vein may be wholly or partially occluded by the thrombus. Later changes such as fibrosis, calcification and even obliteration may occur. The most common change in the liver is atrophic cirrhosis, but atrophy, necrosis and fatty changes may occur. The spleen is enlarged in most instances. Infarcts in the spleen, liver and intestines are often found.

The symptoms are not characteristic. The onset is often sudden with marked ascites and dilatation of the accessory veins of the portal system, hematemesis, variable abdominal pain and general weakness. Bloody diarrhea and enlargement of the spleen are not uncom-

1. Brown: St. Bartholomew's Hospital Reports, 1901, xxxvii, 53-183.
2. Herringham: Allbutt's System of Med., Macmillan & Co., London, 1908, iv, 141-145.
3. Rolleston: Diseases of the Liver, Gall-Bladder, Bile Tracts, W. B. Saunders Co., Philadelphia and London, 1905, 53-56.
4. Lissauer: Virchow's Arch. f. Path. Anat., 1908, cxcii, 278-305.
5. Lewis and Rosenow: Arch. Int. Med., Chicago, 1909, iii, 232-248.

mon findings. If the thrombosis extends into the mesenteric veins the clinical picture may change to one of intestinal obstruction.

Clinically portal thrombosis is rarely diagnosed because of the intimate association with the common causes of portal obstruction. Atrophic cirrhosis of the liver, malignant growths of the stomach, liver, bile passages and pancreas and acute infective processes in the peritoneal cavity are the most common diseases which overshadow the clinical picture of portal thrombosis.

The treatment does not differ from that for atrophic cirrhosis of the liver unless a mesenteric vein is involved and operative procedure is indicated.

The prognosis is unfavorable. Only a few cases have recovered. The duration of the disease usually depends on the associated pathological condition. Fourteen of the thirty-four instances of this disease reported by Brown died within one month.

Case 1.—N. W., aged 36, a housewife by occupation, was admitted to the Cook County Hospital May 30, 1912, on the medical service of Dr. Loeb. She was in a semi-comatose condition and died before any history or examination could be obtained.

The necropsy report was as follows: *Anatomical Diagnosis* (Dr. LeCount): Atrophic cirrhosis of the liver; multiple biliary retention cysts of the liver; chronic fibrous thickening of the peritoneum; thrombosis of the portal vein; marked ascites; anasarca; hydrothorax; dilatation of the veins of the anastomosing points between the systemic and portal circulations; hyperplasia of the spleen; slight chronic diffuse nephritis; extensive hyperplasia of the peri-aortic and intestinal lymphoid tissue; atrophy of the adrenals; compression atelectasis of the lungs; chronic catarrhal gastritis; elephantiasis of the legs; old ulcer of the left leg; ulcerative and disseminated miliary tuberculosis of the lung; fibrous pleuritis; fibrous adhesions between the ileum and urinary bladder, the ileum and the mesosigmoid; the stomach and the colon; the stomach and the mesocolon; the liver and the diaphragm; slight fatty changes in the myocardium; goose fat clot in the chambers of the right heart; anthracotic calcareous tracheobronchial lymph glands; persistent pericarditis; pyosalpinx; marked fatty changes in the kidneys; multiple small ovarian cysts; persistent Eustachian valve; calcareous

thickenings in the leaflets of the aortic valves; fenestrations of the mitral and pulmonic valves; petechial hemorrhages in the skin of the axillae; striae gravidarum.

The thrombus in the portal vein was at the junction of the splenic and mesenteric veins.

Histological examination of the tissues revealed fatty changes and cirrhosis of the liver, senile changes in the kidney, hyperemia of the spleen and lungs, tuberculosis of one lymph gland. No bacteriological findings were recorded.

Case 2.—L. R., a white American female, 35 years of age, was brought to the hospital of the House of Correction Feb. 23, 1914, in a semicomatose condition. Her pulse was rapid and thready. The respirations were rapid and the chest was full of mucous râles. She died Feb. 24, 1914.

Anatomical Diagnosis (Dr. LeCount): Marked atrophic cirrhosis of the liver; generalized slight icterus; marked hyperplasia of the spleen; marked fatty changes of the myocardium, cloudy swelling of the kidneys; mural (non-obliterating) thrombosis of the portal vein; infarcts in the spleen; passive hyperemia in the esophagus and rectum; vascular anastomosis (compensatory) between the omentum and the peritoneum; marked hypostatic hyperemia of the dependent portions of the lungs; passive hyperemia of the kidneys, renal pelves and urinary bladder; moderate edema of the lungs and brain; superficial bruises of the skin of the face and lower extremities; numerous hypodermic needle-puncture wounds of both arms; bilateral blepharites; chronic catarrhal cystitis of the urinary bladder; atrophy of the thyroid and ovaries; fibrous epicardial patches; fibrous thickening of the anterior mitral leaflet; adventitious fibrous adhesions between the lesser curvature of the stomach and the pancreas; slight coal-dust pigmentation of both lungs; striae albicantis of the abdomen; old vaccination scar of left arm; small intersigmoid fossa.

The liver is one-third smaller than normal. It weighs 1,200 grams. Its external surface is very uneven and grossly the liver has all the characteristics of a marked atrophic cirrhosis. In the portal vein and its larger branches in the liver there is a slightly adherent clot which does not completely obstruct the lumen of the vessel. This thrombus does not extend into the mesenteric or splenic veins. The wall of the portal vein is slightly "thickened."

No bacteriological examination was made in this instance.

Histological examination revealed a healing thrombophlebitis of the portal vein. No bacteria could be demonstrated in the wall of the vein or the thrombus.

Case 3.—A laborer by occupation, 33 years of age, suffered repeated attacks of ascites and dyspnea during the past two years. The first attack came on with an acute swelling of the abdomen, dyspnea, and edema of the scrotum. Under treatment these symptoms improved and six weeks later he returned to work. After working one month the ascites recurred, and since then he has had several attacks, each being more severe than the preceding one. The ascites was relieved three times by paracentesis. He had no pain with these attacks. Previous to two years ago his health had

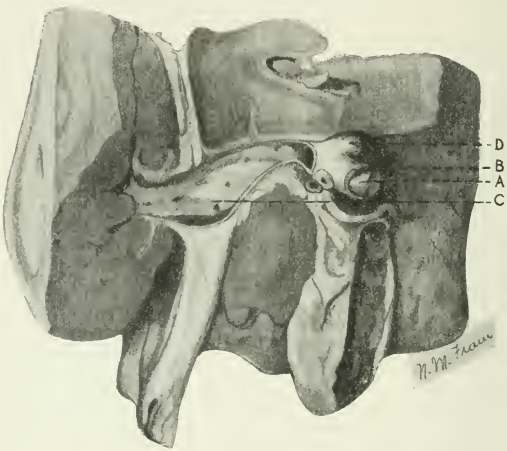

Fig. 1.—(Case 3).—A drawing of the inferior surface of the liver showing the portal vein partially occluded by a thrombus. *A*, thrombus; *B*, wall of the portal vein; *C*, *D*, branches of the portal vein in the liver.

been perfect. He denied venereal infection and alcoholic excess. The family history was negative.

On Dec. 3, 1913, he entered the Cook County Hospital to the service of Drs. Miller and Hamburger suffering from ascites, edema of the lower extremities, and shortness of breath. This attack came on three weeks before his entrance to the hospital. Examination revealed a fairly well nourished middle aged man who seemed quite dyspneic and uncomfortable. Anemia was apparent. Moist râles were

heard over the bases of both lungs. There was a distinct systolic murmur heard best over the apex of the heart. The systolic blood pressure was 175 mm. of mercury, the diastolic 100 mm. The superficial veins of the abdominal wall were enlarged and tortuous. The abdomen was so distended with fluid that nothing could be gained by palpation through abdominal wall. The prostate gland was enlarged. The lower extremities were edematous as high as the knees and there were a few small brown atrophic scars in the skin of the anterior tibial surfaces. Repeated examinations of the urine revealed albumin, hyaline and granular casts and a few red blood cells. Analyses of test meals revealed no free HCl and a combined acidity of 10. Occult blood was found in stomach contents but no sarcinae or Boas-Oppler bacilli. The blood contained 3,348,000 erythrocytes, 2,950 leukocytes and 30 per cent. hemoglobin. Under treatment the ascites and edema decreased and three weeks after entrance another examination of the abdomen was made. There was found in the left hypochondrium a large, firm, smooth, slightly movable mass which was posterior to the colon. Radiographic examination revealed a displacement of the stomach to right of midline by an extra gastric tumor.

Patient gradually improved until Jan. 9, 1914, when he had a sudden attack of pain in the left upper quadrant of the abdomen, a chill, and high temperature gradually subsided and he died an asthenic death Jan. 12, 1914.

Anatomic Diagnosis.—Thrombosis of the portal vein, nearly occluding its entrance into the liver; extensive dilatation and engorgement of the splenic, superior and inferior mesenteric veins; multiple recent infarcts of the spleen; enormous hyperplasia of the spleen; marked passive hyperemia of the large and small intestine; marked ascites; ancient healed (calcareous) endocarditis of the aortic valves, with great deformity of the valvular leaflets; hypertrophy of the myocardium with marked fatty changes; marked passive hyperemia of the lungs; left sero-fibrinous pleuritis; chronic diffuse nephritis (large white kidneys); anemia, sacral decubitis, many gold-filled teeth.

The liver is smaller than normal. It weighs 1,120 grams and its external surface is nodular and has all the gross appearances of an atrophic liver.

The portal vein is enlarged (Fig. 1). It measures 3 cm. in its widest diameter and is almost entirely occluded by a firmly organized blood clot. This blood clot is 6 cm. in length and 2.6 cm. in diameter at its widest portion. It is firmly attached to the wall of the vein around two-thirds of its circumference. Anteriorly there is a very narrow crescentic open-

ing between the thrombus and the wall of the vein. This opening measures 1 mm. in diameter in the widest portion. This clot does not extend into the branches or tributaries of the portal vein. It cuts with resistance and the cut surface has a bluish semitranslucent cortex and a brownish medulla. The main branches of the portal vein in the liver are greatly dilated, especially the left branch, which measures 25 mm. in its widest diameter.

The gall bladder is slightly enlarged. It contains a moderate amount of thick viscid bile, but no concretions. The wall of the gall bladder is slightly thickened. The gall tracts are patent.

Histological examination of the wall of the portal vein and thrombus reveals an organizing mural thrombus and a fibrocalcareous thrombophlebitis.

Under higher magnification numerous clumps of small Gram-positive micrococci arranged in short chains can be seen in the wall of the portal vein and meshes of the thrombus.

Case 4.—M. C., aged 26, a housewife by occupation, entered the Cook County Hospital to the service of Dr. H. F. Lewis, Jan. 4, 1915. She was in a comatose condition and a history was obtained from friends. Three weeks before this time she gave birth to a full term infant. The placenta did not come away for some time so the midwife delivered it with forceps. There was no excessive hemorrhage. She got up on the second or third day and was apparently recovering normally until three or four days ago when she became ill. She complained of abdominal pain, increasing weakness and fever. These symptoms have increased until now she is in a comatose condition. Examination was practically negative except for a coated tongue, fetid breath, slight symmetrically enlarged heart, tender, distended and rigid abdomen, and a lacerated cervix. The urine was practically negative. No blood examination was made. In the hospital her condition gradually became worse. She vomited and complained of chilliness. Her temperature was slight, reaching 103 F. twenty-four hours before death. She rapidly became weaker and died Jan. 7, 1915.

The necropsy report was as follows: Anatomic diagnosis (Dr. LeCount). Puerperal uterus and mammae; corpus luteum of pregnancy in one ovary; gangrenous decidual endometritis; "primary" thrombosis of the portal vein; descending thrombosis of the mesenteric and splenic veins; infarction of part of the small bowel with extensive necrosis; blood in the bowel; generalized acute sero-fibrinous peritonitis; slight hemo-peritoneum; mottled clots ("ante-mortem") in

the left renal vein; marked cloudy swelling of the renal parenchyma generally; general anemia; slight anasarca; venesection and hypodermic needle puncture wounds of both arms; hot water burn on inner anterior surface of the right leg; hyperplasia of the thyroid gland; lineae nigra and striae albicantes of pregnancy of the abdomen; slight hyperplasia of the spleen; bronchopneumonia; slight hydrothorax; slight fatty changes in the intima of the carotids at their bifurcation; poorly kept teeth, several caseous and several missing; ill kept and broken finger nails; coal dust pigmentation, tracheobronchial lymph glands; marginal emphysema.

On opening the main part of the portal vein there is seen a grey occluding clot totally occupying the lumen of the vein which is enlarged thereby. This clot is continuous with the clot in the mesenteric veins.

Bacteriologic examination by Dr. E. C. Rosenow of material from the center of the thrombus revealed peculiar streptococci producing rather large, moist, greenish colonies on blood agar plates, large gram positive bacilli and many colon bacilli. Anaerobic cultures made by Dr. Moody revealed a fusiform bacillus, a large pigmented bacillus, a streptococcus and *Bacillus aerogenes capsulatis.*

Histological examination of the portal vein was not made in this instance.

As a possible explanation of the pathogenesis of the infective portal thrombosis in the third and fourth examples, it seems reasonable to assume that the original foci of infection were in the endocardium of the aortic valve and the puerperal uterus.

Feb. 8, 1915.

COMPLEMENT FIXATION IN HODGKIN'S DISEASE

J. J. MOORE

(From the Department of Experimental Medicine, University of Illinois, Chicago)

In 1913, Bunting and Yates[1, 2] described the isolation of a pleomorphic diphtheroid organism from the lymph glands in four out of seven cases of Hodgkin's disease and concluded in 1914[3] that "Hodgkin's disease is an infectious disease due to a diphtheroid organism,

1. Bunting and Yates, Arch. Int. Med., 1913, xii, 236.
2. Bunting and Yates, Jour. A. M. A., 1913, lxi, 1803.
3. Bunting, Bull. Johns Hopkins Hospital, 1914, xxv, 177.

the Bacterium hodgkini." Previous to this Fränkel and Much[4] found a somewhat similar organism in stained sections of glands in this disease. Negri and Mieremet[5] were the first to cultivate the organism. Subsequently Billings and Rosenow[6] confirmed these findings and successfully cultivated the organism from the blood in a few cases.

Early in 1914 we commenced immunizing a horse with cultures of organisms isolated from glands in cases of Hodgkin's disease. Endeavoring to find an efficient method to ascertain the potency of the serum, we tried agglutination, opsonic counts and precipitation with negative results. Since complement fixation with bacterial antigens has been successful in gonorrhea, pertussis and typhoid fever, we eventually employed it in testing the immune serum.

Both polyvalent and single strain antigens were prepared. The cultures were grown on Loeffler's serum agar for twenty-four hours to four weeks. The bacteria were washed and centrifugated in sterile normal saline solution three times and then preserved in sterile normal salt solution to which 0.5 per cent. phenol had been added as a preservative. The various antigens were tested for their minimum anticomplementary dose and one-fourth to one-half of this used in the tests of the patients' sera. Sixteen strains of organisms isolated from the glands and blood in cases of pseudoleukemia were obtained through the kindness of Drs. Rosenow and Garde.

In addition to antigens, prepared from Bacterium hodgkini (Bunting and Yates), we had as controls antigens of staphylococci, streptococci, B. coli, and diphtheroid bacilli. The diphtheroid bacilli were isolated by me from lymph glands in chronic arthritis and resembled those found in Hodgkin's disease, both morphologically and culturally.

Both antihuman and antichicken hemolytic systems were employed in the experiments.

The sera of seven patients with Hodgkin's disease have been subjected to the tests. In all of these, histo-

4. Fränkel and Much, Ztschr. f. Hyg., 1910, lxvii, 159.
5. Negri and Mieremet, Centralbl. f. Bakteriol., 1913, lxviii, 292.
6. Billings and Rosenow, Jour. A. M. A., 1913, lxi, 2122.

logical examination of diseased glands has confirmed the clinical diagnosis, and cultures from the majority of these have resulted in the growth of a pleomorphic organism. The tests have been made at irregular intervals upon two patients for a period of over five months; one case for three months; one for two months; two for one month; and in one patient who succumbed to the disease but one test was made. In every test the reaction was negative.

Since all these patients were receiving autogenous or mixed vaccines we were interested in noting whether complement fixing bodies would be produced. In one instance the first test was made before any vaccine was administered, the second test after nine doses of vaccine. In another patient one injection of vaccine preceded the first test. Others had from seven to ten doses of vaccine before the first test and over fifty before the last test. The dose of vaccine varied from 10 million to 1 billion. The complement fixation reaction was negative in all cases.

With one patient, in addition to the polyvalent antigens, we repeatedly used a homologous antigen (one prepared from the organism isolated from the individual's own glands). This likewise resulted in complete hemolysis.

For control sera the following diseases were tested: myelogenous leukemia, four cases; lymphatic leukemia, two cases; lymphosarcoma, two cases; tuberculosis, two cases; syphilis, two cases; asthma, two cases; chronic arthritis, one case; normals, three cases. The leukemias were selected from their close relationship to Hodgkin's disease; the lymphosarcomas for similar reasons and as organisms similar in all respects to those isolated in pseudoleukemia were cultured from the glands; tuberculosis and chronic arthritis because similar organisms have been isolated in these diseases; asthma on account of the eosinophilia; syphilis to ascertain if a positive syphilitic blood was also positive with these bacterial antigens. In one case of lymphosarcoma autogenous vaccine was administered over forty times, complement fixation tests were made four times during a period of three months. In this

case as in all the other control tests no inhibition of hemolysis resulted. The other bacterial antigens likewise caused hemolysis in every instance.

In direct contrast to the lack of positive results in individuals having the disease is the reaction of the blood from an immunized horse. I previously mentioned that a horse had been immunized with these organisms. This animal has been receiving enormous doses of dead and living organisms subcutaneously and intravenously for over eight months. The tests upon the sera of the immunized and control horses differed from those upon the human sera in that three and four times the hemolytic titer of the complement was used instead of two as in the latter. This was because the sera of horses were found to contain more complement binding substances than human sera.

One-tenth c.c. of the specific antigen with 0.0005 of immune serum produced complete inhibition of hemolysis. Other bacterial antigens with the same serum produced hemolysis. Four control horses gave negative results with all antigens.

I wish to thank Drs. Billings, Rosenow, Garde and Horn for their kind assistance during these experiments.

Feb. 8, 1915.

SOME STUDIES WITH REGARD TO PROCEDURES INFLUENCING THE INFLAMMATION PRODUCED BY MUSTARD OIL

I.—W. B. McCLURE AND P. S. CHANCELLOR
II.—S. AMBERG AND A. S. LOEVENHART
(From the Otho S. A. Sprague Memorial Institute Laboratory of the Children's Memorial Hospital, Chicago)

I. Sodium iodoxybenzoate and sodium iodosobenzoate administered intravenously in proper dosage inhibit completely or nearly completely the edema produced by installation of mustard oil in the conjunctival sac of the rabbit. The same effect is produced by intraperitoneal injection, whereby the iodosobenzoic acid is given as such, in suspension, owing to the irri-

tating action of sodium iodosobenzoate solution on the peritoneum.

Sodium iodbenzoate has no inhibiting action. When the edema is well under way administration of sodium iodoxybenzoate and sodium iodosobenzoate have no definite effect. Neither was it possible to inhibit the edema by local application of sodium iodoxybenzoate.

These substances do not seem to belong to the groups of substances described by Januschke as having an inhibitory effect on the edema of the mustard oil conjunctivitis, either having an influence on the sensory nervous apparatus or on the vessels in the sense of altering their permeability.

Intravenous injection of urethane leading to deep narcosis in rabbits retards the onset of the edema which in the course of time seems to develop fully. The same effect has been noted in animals deprived of about one-third of their total amount of blood.

The intravenous administration of sodium cyanide did not give uniform results, perhaps owing to the difficulty of finding the proper dosage. Of twelve animals, three showed a definitely more marked reaction than the controls, in two other instances this excess was less marked, in four cases the reaction was equal and in three cases the reactions of the controls were more pronounced.

A series of experiments was undertaken to see whether the inhibition produced by sodium iodoxybonzoate could be overcome by administration of HCN or sodium cyanid. Only in three experiments did there seem to be a marked diminution of the inhibitory effect of the sodium iodoxybenzoate. In a number of other experiments the results were either indefinite or negative.

II. The effect of benzoylperoxid on the mustard oil inflammation of the rabbit's eye was studied by administering this substance in suspension intraperitoneally. In some instances the edema could be inhibited nearly completely in this manner. In similar experiments phthalic acid peroxid inhibited the edema during the life of the animals (2-4 hours), but they died of a hemorrhagic peritonitis. Control animals receiving

intraperitoneally corresponding doses of sodium benzoate or sodium phthalate showed some inhibition of the edema although this inhibition was much less pronounced. In some experiments where the sodium salt of phthalic acid peroxid was given intravenously and the mustard oil intracutaneously, a definite inhibition of the reaction was noted, lasting for several hours. Benzoylperoxid and phthalic acid peroxid contain their active oxygen in a combination different from that in iodoxy- and iodosobenzoic acid and both blue tincture of guaiacum directly, the phthalic acid peroxid being the more active of the two substances. Oxygen as gas administered intraperitoneally had no influence on the intracutaneous mustard oil reaction, while sodium iodate and sodium periodate administered intravenously exercised some diminishing effect. In a series of experiments rabbits were kept under diminished partial pressure of oxygen, varying in different experiments from about 9 to 12 per cent. The atmospheric pressure was not changed. The animals received an intracutaneous injection of mustard oil after being kept in an atmosphere with reduced oxygen tension for varying periods of time up to 84 hours, or before being exposed to such an atmosphere. The reactions did not show sufficiently marked differences from those of the controls to justify any conclusions.

Feb. 8, 1915.

LARGE CONGENITAL CYSTIC KIDNEYS

WAYNE W. BISSELL

(From the Pathological Laboratory of Cook County Hospital)

J. N., a Swedish teamster, 44 years of age, entered the Cook County Hospital on September 11, 1914, to the service of Drs. Grinker and Krumholz, suffering from congenitally cystic kidney previously observed and demonstrated before the Chicago Medical Society by Dr. Charles Spencer Williamson.

On admission he complained of indefinite and irregular dyspepsia, headache, dizziness and some difficulty in walking due to two "strokes of apoplexy" during the previous five years. Examination revealed a well nour-

ished man and aside from evidence of an old hemiplegia, a large mass was visible and palpated in the upper abdomen. This was bilateral, taking the position of the kidneys and so large that on the right side it extended down nearly into the pelvis. It was firm, nodular, indistinctly fluctuating, behind the colon, liver, spleen and stomach and from the history known to have been present for several years and stationary as far as growth was concerned. The urine constantly contained blood. The blood pressure was as high as 200. With increasing anemia and emaciation he finally passed into coma which was apparently uremic and died on October 20, 1914.

Post-mortem examination.—Permission was gained to open the abdomen and at autopsy, kidneys were removed that possessed no features differing materially from other specimens of congenital cystic kidneys other than their great size. The right was slightly larger than the left, measuring 23 cm. from pole to pole, 15 cm. through the sagittal section and 14 cm. in thickness. Together they weighed 4,030 g.

Feb. 8, 1915.

COR BOVINUM WITH AN ANEURYSM OF THE ASCENDING AORTA

WAYNE W. BISSELL
(From the Pathological Laboratory of Cook County Hospital, Chicago)

M. M., a Mexican laborer, 45 years of age, returned to Cook County Hospital on November 11, 1914, to the service of Drs. Miller and Hamburger, complaining of shortness of breath and swelling of the lower extremities; he had been discharged two weeks before.

He was a fairly well nourished man past middle life, suffering marked dyspnea. The pulse was distinctly of the "water-hammer" type and there was marked pulsation of the carotid arteries. The heart was found to be greatly enlarged in all dimensions with systolic murmurs over the aortic area and at the apex. A distinct thrill could be felt over the upper sternum and over the vessels of the neck. There was a pulsation easily felt in the suprasternal fossa but no tracheal

tug could be detected. No changes were found in the blood or urine. The blood pressure was as high as 190; with an increasing general anasarca, death occurred on January 22, 1915.

Anatomic Diagnosis.—Marked, healed syphilitic aortitis; marked deformity of the aortic valvular leaflets (syphilitic aortitis?); sacculated aneurysm of the aorta just above the left sinus of Valsalva; huge hypertrophy and dilatation of the myocardium (cor bovinum); anomalously placed mouth of the right coronary artery; marked anasarca of the lower extremities, penis, scrotum and hands; moderate ascites;

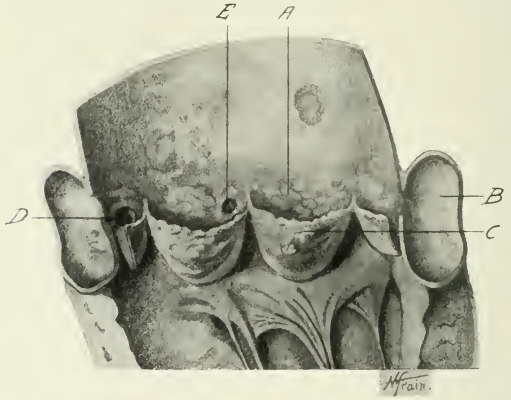

Fig. 1.—The aortic ring in an example of aneurysm of the ascending aorta and cor bovinum. *A*, circumferential fibrous aortitis (syphilitic) *B*, half of the aneurysmal sac; *C*, fibrous thickening of the semilunar valves; *D*, dilated left sinus of Valsalva; *E*, anomalously located mouth of the right coronary artery.

marked right hydrothorax; left fibrous adhesive obliterative pleuritis; chronic diffuse nephritis, small red kidneys; marked chronic passive hyperemia of the liver; marked hyperplasia of the tracheo-bronchial lymph nodes; muco-purulent tracheo-bronchitis; fibrous adhesions between the gall bladder and duodenum.

The heart is very large; emptied and stripped of pericardium it weighs 1,200 g. There is distinct enlargement of the root of the aorta which bulges forward pressing on

the pulmonary artery. On opening the left ventricle into the aorta this is found to be a sacculated aneurysm of the ascending aorta opening into it by an orifice 25 mm. in diameter above the left sinus of Valsalva. This aneurysm is ovoid in shape, 5 cm. in its vertical dimension and 3 cm. in diameter. The left semilunar valve is greatly thickened, calcareous and deformed, making accurate closure of the ring impossible. The contiguous portions of the right and left semilunar valves have apparently fused to make a dense wall common to the two. The mouth of the left coronary artery is dilated to a diameter of 1 cm. and the artery is patent throughout. The aneurysm wall is thick, stiff, fibrous and studded with many slightly elevated nodules on its intima side. This nodular thickening lines the first portion of the aorta. The mouth of the right coronary artery opens into the extreme left portion of the right sinus of Valsalva. The myocardium of the left ventricle measures 25 mm. through its thickest portion (Fig. 1).

Feb. 8, 1915.

ACUTE THROMBO-ULCERATIVE ENDOCARDITIS OF A BICUSPID AORTIC VALVE

WAYNE W. BISSELL

(From the Pathological Laboratory of Cook County Hospital, Chicago.)

E. D., a Polish housewife, 52 years of age, entered the Cook County Hospital on September 11, 1914, to the service of Drs. Butler and Patton. She was in a delirious condition and no history was obtainable. Examination revealed a well nourished, somewhat anemic woman apparently past middle life and seriously ill. No abnormalities were discovered in her head or neck. The heart was slightly enlarged to the left and at the apex a harsh systolic murmur was heard, which was transmitted to the axilla. The temperature was of an irregular type, varying between 98 and 104.2 F. The liver and spleen were distinctly palpated. The blood contained as high as 30,600 leukocytes per c.mm., 3,600,00 erythrocytes and hemoglobin to the per cent. of 60. No agglutination was noted in the Widal examination. On two occasions the Streptococcus mucosus capsulatus was isolated from the blood; during the last few weeks a definite

systolic murmur over the aortic area and slight general icterus developed; death occurred on October 18, 1914.

Anatomic Diagnosis.—Marked acute thrombo-ulcerative aortic endocarditis; bicuspid aortic valve; multiple minute hemorrhages of the epicardium and of the root of the aorta; marked hypertrophy of the myocardium of the left ventricle; nodular calcareous sclerosis of the aorta; coal dust pigmentation of the tracheobronchial lymph nodes and of the

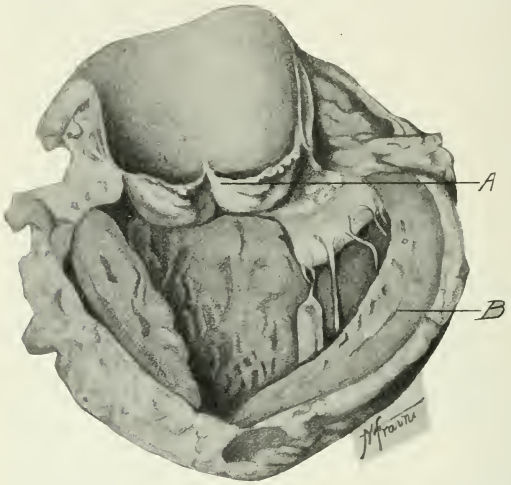

Fig. 1.—Acute thrombo-ulcerative endocarditis of a bicuspid aortic valve. *A*, thrombo-ulcerative lesions; *B*, slight hypertrophy of the myocardium.

lungs; marked arteriosclerosis of the kidneys; marked passive hyperemia of the kidneys; marked atrophic cirrhosis of the liver; cholelithiasis; marked fibrous cholecystitis; marked hyperemia of the spleen; moderate bilateral hypostatic hyperemia of the lungs; fibrous adhesions between the fundus of the uterus and rectum; moderate general icterus; multiple spinal puncture wounds; slight anasarca of the legs below the knees; striae gravidarum over the abdomen; slight

diastasis recti; small sacral decubital necrosis; bruise of the right thigh; moderate emaciation; slight general icterus.

"This heart is moderately enlarged through hypertrophy of the left ventricle. The aortic ring contains but two semilunar valves, well formed and the seat of an acute thrombo-ulcerative endocarditis. Both coronary arteries open into the aorta adjacent to the semilunar valve which takes the usual position of the right semilunar" (Fig. 1).

On account of the apparent short duration of the endocarditis and the perfect formation of these valves it seems reasonable to assume that this lack of a third cusp to the aortic ring is a congenital anomaly. Further, with the absence of any marked hypertrophy of the myocardium of the left ventricle or any marked dilatation of the mitral ring, it might be suggested that before the endocardial infection took place this aortic valve was perfectly competent. The presence of thrombo-ulcerative endocarditis of a bicuspid aortic valve is also very well known.

Feb. 8, 1915.

ANEURYSM OF THE ARCH OF THE AORTA WITH BILATERAL COMPLETE INFARCTION OF THE KIDNEYS

WAYNE W. BISSELL

(From the Pathological Laboratory of Cook County Hospital, Chicago)

L. C., a colored laundress, 50 years of age, entered the Cook County Hospital July 20, 1914, to the service of Drs. Morf and Keyes, complaining of pain in the right lumbar region radiating to the spine and anteriorly to the abdomen. She stated that this pain had come on suddenly ten days previously and although very sharp at the onset was now of a heavy, aching character. She also said she had recovered from a similar attack four months previous to admission. Associated with this attack she had noticed that her urine was very turbid and scanty in amount. Three days previous to entrance she became nauseated and had since vomited several times daily. There were no other noteworthy points of history gained.

On examination the patient was well nourished and apparently suffering an acute illness. There were no abnormalities discovered in the heart or lungs. The abdomen was distended and tympanitic. There was some rigidity of the right hypochondrium and slight

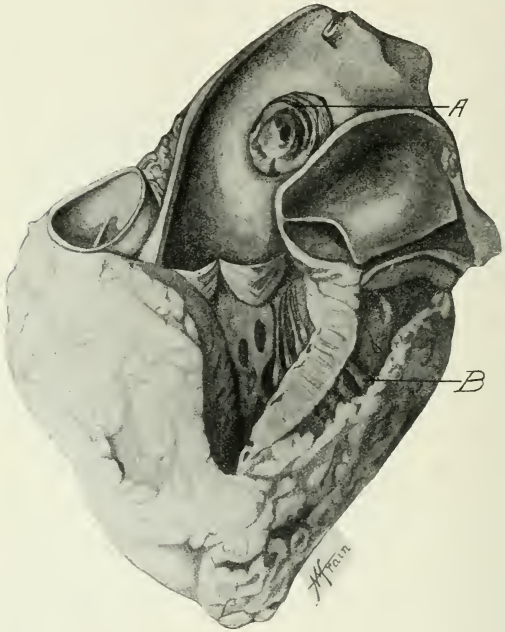

Fig. 1.—Aneurysm of the arch of the aorta with bilateral complete infarction of the kidneys (Fig. 2). *A*, opening of the aneurysm into the aorta, clotted blood presenting; *B*, fibrous obliterative pericarditis.

tenderness to deep pressure. The right lumbar region over the kidney was very tender. The urine was small in amount, cloudy and contained a great deal of blood. There was a polymorphonuclear leukocytosis of 46,000.

The temperature varied between 101 and 102.8 F. Radiographic examination was not made. On July 22, 1914, an exploratory nephrotomy was done, but with failure to discover the lesion and after a progressively downward course she died on August 1, 1914.

Anatomic Diagnosis.—Stellate scars in the capsule of the liver; scars on the shins; nodular sclerosis of the aorta and its main branches; obliterative fibrous adhesive pericarditis; sacculated aneurysm of the arch of the aorta; obliterative thrombosis of the aneurysmal sac; bilateral complete infarction of the kidneys; recently shaven pubic hair; recent

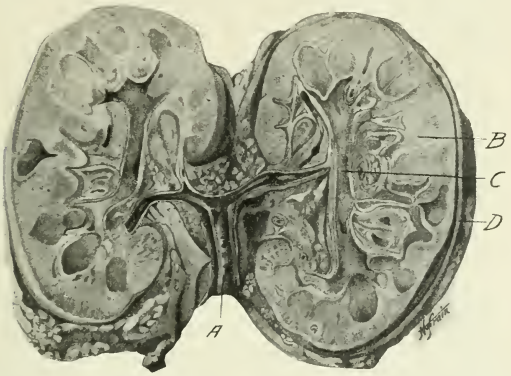

Fig. 2.—Complete infarction of a kidney. *A*, thrombus completely occluding the renal artery; *B*, dry, swollen parenchyma; *C*, diffuse submucous hemorrhage in the pelvis; *D*, edematous capsule.

repaired right nephrotomy wound; atrophic striae gravidarum; moderate hemorrhage into the tissues about the right kidney; hypodermic puncture needle wounds of both arms; marked sacral decubitus; marked fatty changes in the liver; marked cloudy swelling of the liver and myocardium; moderate hyperemia of the dependent portions of both lungs; fibrous adhesions between the mesosigmoid and the fimbria of the left tube, between the gall bladder and the colon and about the appendix.

A description of the heart and kidneys is as follows:

"This heart is slightly enlarged. The pericardium is firmly adherent to the epicardium obliterating the pericardial sac. There are no noteworthy alterations in the myocardium or valves. There is a sacculated aneurysm of the ascending portion of the arch of the aorta pointing downward beneath the arch and 4 cm. in diameter. Its opening into the aorta is 2 cm. in diameter and annular. The sac is filled with coagulated blood (Fig. 1). The kidneys with their capsules are enlarged, weighing 420 g. The right is the larger, weighing 230 g. The renal arteries take origin in the normal way, as separate branches of the aorta and each is completely occluded by an adherent, firmly organized thrombus which extends into the smaller branches as far as they can be followed with the scissors. The capsule of the right kidney is very swollen and edematous and the seat of many hemorrhages. Externally the cortical tissue is also the seat of disseminated small hemorrhages. The interior is dusky brown, very dry and swollen. The calices of the renal pelvis are red with diffuse submucous hemorrhage. The left kidney is similar to the right except that the changes do not seem to be so intense" (Fig. 2).

Feb. 8, 1915.

HUGE GUMMA OF THE SPLEEN

WAYNE W. BISSELL

(From the Pathological Laboratory of Cook County Hospital, Chicago.)

J. B., a Polish laborer, 32 years of age, was admitted to the Cook County Hospital on Dec. 18, 1913, to the service of Drs. Williamson and Bloch. He stated that he had been ill for three months with pain in the left lumbar region, dull aching in character and of such severity as to keep him from work. His sleep was often disturbed at night, due to sharp pain caused by movement. Associated with this pain he had noticed considerable tenderness in the left flank, general progressive weakness and some fever.

Examination revealed a well nourished man apparently in pain and suffering a marked furunculosis. In the abdomen there was a hard, tender mass occupying the position of the spleen, lying in front of the stomach and colon and pushing them to the right, extending downward to a level 3 cm. below that of the umbilicus and definitely notched on its firm, rounded lower bor-

der. His temperature was slightly elevated; at one time as high as 100.8 F., and his blood contained as many as 10,800 leukocytes. Radiographic examinations were made and corroborated the clinicians' observations on the size and position of the tumor mass. Syphilis was denied and one Wassermann reaction was negative.

After very careful study of this condition no further data were gained that had bearing on a diagnosis and on Jan. 27, 1914, he was transferred to the service of Drs. Andrews and Speed for an exploratory laparotomy.

Microscopic preparations of tissue removed at operation were of no aid to diagnosis and after progressive

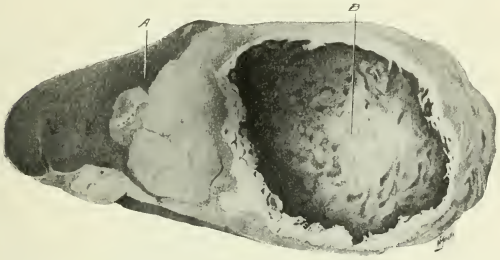

Fig. 1.—Huge gumma of the spleen. *A*, miliary gumma in the spleen substance; *B*, excavation of the softened center of the enormous gumma.

emaciation and anemia he died on March 12, 1914. While the clinical diagnosis was by no means a settled one, that of Gaucher's disease seemed to be most favored.

At autopsy on the date of death the anatomic diagnosis was as follows:

Anatomic Diagnosis.—Malignant (?) tumor of the spleen extending into the greater curvature of the stomach, the splenic flexure of the colon and the pancreas; metastatic malignancy (?) in the lateral lumbar and retro-aortic lymph nodes both above and below the diaphragm; emaciation; marked anemia; ascites; moderate bilateral hydrothorax; hypodermic needle puncture wounds of both arms; marked

bilateral bronchopneumonia; cyanotic induration of the kidneys; miliary gummata (?) of the liver.

"This spleen weighs 1,760 gm. It is adherent to, but quite easily separated from the colon, stomach and pancreas. The omentum is firmly adherent to the greater part of its anterior surface. Approximately the upper four-fifths of this spleen has been replaced by a tumor mass which is gray-white in color, deeply fluctuating in consistency and on section so softened in the center that its contents escape freely leaving an excavation 13 cm. in diameter, half the size of the tumor itself. The wall of this softened center is apparently made up of fibrous tissue and its inner surface is shaggy with necrotic debris which resembles fibrin. In the spleen substance adjacent to the sharply circumscribed tumor mass there are a few pearly tubercular lesions resembling gummata (Fig. 1). A few similar nodules are seen in the liver."

Microscopic preparations were made from blocks of tissue taken from the wall of this mass and from the spleen. The wall is made up of heavy bands of hyalin fibrous tissue traversed by thick-walled blood vessels and on the inner side there is some round cell infiltration. The small tubercles both in the spleen and the liver are miliary gummata, many of them possessing giant cells.

Feb. 8, 1915.

REPORT OF TWO CASES ILLUSTRATING THE POLYGLANDULAR SYNDROME

HARRY JACKSON

(From the Pathological Laboratories of Northwestern University Medical School, Chicago.)

In 1899 Rogowitsch first suggested the polyglandular syndrome by observing the increase in size of the hypophysis after removal of the thyroid gland. Since then, many disturbances coincidentally involving two or more of the glands of internal secretion have been recorded. I wish to record two such cases coming under my observation.

Case 1.—*Hyperplasia of Thymus and Hypophysis with Atrophy of Pineal Gland.*

Clinical History.—Male, 21 years of age, a native of Greece and a laborer by occupation, entered the County Hospital on the neurologic service of Dr. Grinker. Because of the disturbed mental condition of the patient only a meager history is obtainable. For the past year he has suffered from headaches, dizziness and pain all over the head. There had been no vomiting previous to entrance to hospital. During the past few months his vision has been gradually failing. His past history is negative. He had never been sick before, does not use alcohol to excess, and denies venereal disease. Physical examination discloses a young white man somewhat

Figure 1

emaciated who can move about fairly well but is quite weak. He is apathetic and only answers questions when aroused and then relapses into stupor again. His head is quite sensitive to the touch. His pupils react slightly and sluggishly. They are enlarged and equal. The patient cannot see to count his fingers. The ears, neck, chest, abdomen and genitalia are negative. The reflexes at the knee are somewhat increased and there is a suggestion of a Babinski. There is moderate ataxia and a slight Romberg. The urine is negative. A spinal puncture gives 8 c.c. of a clear fluid which is negative to Wassermann, Nonne and Noguchi tests. Ophthalmoscopic examination reveals a bilateral secondary optic

atrophy. The vessels are tortuous and the disk border is indefinite. The nurses' reports since his entrance state that the patient continually groans with pain in the head, has emesis of milk and talks continually. On entrance his temperature was 98 F., pulse 88 and respiration 20. The next day temperature was 102.8 F., pulse 88 and respiration 20. He died Feb. 8, 1914, and autopsy was performed Feb. 9, 1914. The clinical diagnosis of brain tumor was made. A Roentgen-ray picture could not be obtained before death and the tumor could not be localized.

Autopsy Protocol.—The body is that of a slightly developed white man about 20 years of age.

The skull cap is greatly thinned, being 1 mm. in thickness over the parietes and 8 mm. thick at the thickest part posteriorly. It shows the imprint of the convolutions of the brain on its inner surface. The dura is opaque and thickened in spots. A large tumor is present in the region of the hypophysis (Fig. 1). It is trilobate, one lobe occupying the enlarged sella turcica, the second projecting forward between the parietal lobes and hollowing out a place for itself in the frontal lobes. This lobe causes marked pressure atrophy of the optic chiasm and olfactory tracts. The third lobe projects backward and lies between the temporal lobes and rests posteriorly upon the corpora quadrigemina. The sella is enlarged generally to about five times its normal dimensions and is greatly thinned but not perforated. It measures 3 x 3 x 2 cm. The hypophysis tumor when removed is seen to be well circumscribed and covered with a capsule and measures 5½ cm. in length, 4 cm. in height and 3¾ cm. in thickness. On section it is seen to be homogeneous, and of a pale gray color. There are petechial hemorrhages scattered through its substance. The anatomic diagnosis is hyperplasia of anterior lobe of hypophysis.

The brain weighs 1,550 gm. and shows a general hyperemia of its vessels. The foramina of Monro are occluded and there is present marked hydrocephalus internus. Otherwise the brain shows no gross abnormalities except that the pineal gland has undergone almost complete pressure atrophy. On opening the chest one notes a greatly enlarged thymus occupying the anterior mediastinum (Fig. 2). This is composed of two lobes triangular in outline, the base of the triangle being uppermost and the apices of each meeting over the auricles of the heart. Each lobe measures 9 x 4 x 3 cm. and is covered with a thick capsule. The tissue is grayish in color and firm in consistency. Cut section shows very little adipose tissue and dense lymphoid tissue. Its weight is 80 gm.

The heart is enlarged and shows moderate hypertrophy and dilatation. The thyroid is decreased in size and shows very little colloid.

The lungs show spots of fetal atelectasis and hypostatic congestion of both lower lobes.

The liver shows perihepatitis, passive congestion and fatty changes and weighs 1,540 gm.

Figure 2

The spleen shows a perisplenitis and passive congestion. It is somewhat decreased in size and weighs 140 gm.

The kidneys together weigh 340 gm. and show an acute diffuse nephritis of parenchymatous and hemorrhagic types. The adrenals, pancreas, stomach and intestines show no gross changes. The genitalia are normally formed and pubic hair

is present. There is no general increase of fat and the body is normally proportioned. The lymph glands are not enlarged.

Microscopic Examination of Tissues.—Sections taken from different parts of the tumor of the hypophysis all show the alveolar structure of the anterior lobe of the hypophysis. There is marked hyperplasia of the epithelial cells whose nuclei stain deeply. The cytoplasm is neutrophilic, the type of cell being the Hauptzellen of Erdheim. There is very little stroma between the alveoli and the blood vessels are hyperemic. There is no demonstrable remnant of the posterior lobe or intermediary body or infundibulum.

Section from the thymus shows the great mass of it to be made up of densely packed lymphoid cells. There is very little adipose tissue and what is present is at the periphery of the gland and seems to be invaded by lymphoid tissue. The latter occurs in large nodules at the periphery (cortex) and is made up for the most part of densely packed mononuclear lymphocytes. The central portions (medulla) are not so densely packed and have a width equal to that of the cortex and contain many corpuscles of Hassall in a state of hyaline degeneration and greatly enlarged.

The pancreas appears to be generally hyperplastic, the nuclei stain deeply and the vessels are hyperemic. The islands of Langerhans are not numerous and show moderate hyperplasia.

In the spleen the lymphoid elements are decreased. The liver shows marked fatty degeneration.

Case 2.—*Hyperplasia of the Thymus and Islands of Langerhans of the Pancreas with Beginning Exophthalmic Goiter.*

Clinical History.—Seen by Drs. Richter and Beifeld. Mrs. K., aged 49, native of Germany, married and has two children. Mother died of tuberculosis at 30 years. Father died of pneumonia at 50 years. Has three living sisters. As to her previous history she has had colicky attacks since she was 20 years old. About four years ago she had a severe abdominal attack lasting three weeks. These attacks recurred every now and then till the present time. She has also had chronic arthritis of knee joints. For the last eight weeks she has had a miserable feeling in abdomen and has been in bed the last three weeks. During the last week the stools became clay colored and there has been incessant vomiting and symptoms of severe toxemia. There has been no blood in stool or vomitus. She has lost considerable weight. Menstruation has not been regular the last two years. Temperature ranges from 98 to 100; pulse, 100 to 130. The

urine shows a trace of albumin and an occasional hyaline cast. Spinal fluid is negative to Noguchi and Nonne tests. The blood shows 4,400,000 reds, hemoglobin, 79 per cent. The whites number 6,000 of which there are 39 per cent. lymphocytes of the small type, 3 per cent. large mononuclears and 58 per cent. polymorphonuclears. A second count made before death gave 8,000 whites with 62 per cent. small lymphocytes and 36 per cent. polymorphonuclear leukocytes. The thyroid became enlarged the last three weeks and there was tachycardia and tremor and beginning exophthalmos. The clinical diagnosis of acute hyperthyroidism was made.

Autopsy Protocol.—The body is that of a fairly well nourished woman apparently 50 years of age. The thyroid is considerably enlarged in all three lobes and is about five times the normal size. It surrounds the trachea like a collar. Cut section shows greatly increased colloid. Microscopically, the alveoli appear large and filled with colloid which stains deeply. The epithelial cells lining the alveoli are low. There is little stroma and moderate congestion. Here and there, scattered through the substance of the gland are islands of hyperplastic epithelial tissue. The epithelial cells are cylindrical in shape and fill the alveoli. Surrounding such an island the alveoli show beginning papillary ingrowths of the epithelial lining and a reduction in the colloid content of the alveolus, with failure to take a characteristic stain at the periphery. The vessels in such areas show marked congestion. These islands are characteristic of exophthalmic goiter.

The thymus is increased in size, measuring 8 x 6½ x 2 cm. and weighs 40 gm. It lies in the anterior mediastinum above the auricles of the heart and partly covers them. It is soft and fatty, light yellow in color and oblong in shape. Microscopically one notes that about half its substance is made up of the lymphoid tissue. The lymphoid tissue stains deeply and is irregularly scattered through the fat. With low power magnification the nodules of lymphoid substance show a dense periphery (cortex) and a lighter staining central portion (medulla). There are many corpuscles of Hassall in the latter area which have undergone hyaline degeneration and some increase in size.

The pancreas on microscopic examination shows some increase in interstitial tissue. The alveoli are somewhat shrunken; one notes the striking increase in the size of the islands of Langerhans. They are enlarged to two or four times their normal size and are made up of cells whose nuclei stain deeply and which appear to be undergoing active hyperplasia. The capillaries of these islands show marked congestion.

The intestines and lymph glands show no increase in lymphoid elements.

The heart shows moderate fatty infiltration and cloudy swelling and hypertrophy and dilatation. There is moderate hypostatic congestion and edema of the lungs.

The stomach is contracted and negative. The duodenum is negative. There is a chronic appendicitis, chronic arthritis of left knee joint, chronic cholecystitis and cholelithiasis. The spleen is enlarged and shows some increase in its lymphoid elements. The adrenals show no gross changes. The liver shows marked fatty degeneration. The kidneys show an acute parenchymatous nephritis superimposed upon a chronic diffuse nephritis. The ovaries are sclerotic. The head was not opened.

We have, then, two cases with hyperplastic thymus, that have either persisted from childhood or become revivified from a "rest." One is associated with a hyperplasia of the anterior lobe of the hypophysis, the other with a beginning exophthalmic goiter and a marked hyperplasia of the islands of Langerhans of the pancreas. What these changes signify in the metabolism of the individual I shall not attempt to define.

It is interesting to note that in the first case of thymus and hypophysis hyperplasia, there were no clinical symptoms of status lymphaticus, acromegaly, gigantism, genital disturbance or adiposity. Did the hyperplastic hypophysis induce a compensatory growth in the thymus or vice versa or were they both dependent upon a third factor?

In the second case I believe that the pancreas and thymus hyperplasia preceded the changes in the thyroid. In this case the high lymphocytosis and the tachycardia may have been due to the hyperplastic thymus. Could the chronic infections of the joints, appendix and gall bladder have been responsible for the changes effected in the thymus, pancreas and thyroid?

These cases occurred in adults at a time when the thymus normally becomes an atrophic organ.

March 8, 1915.

THE EFFECTS OF EPINEPHRIN INFUSION UPON THE VASOMOTOR APPARATUS (PRELIMINARY REPORT)

R. G. HOSKINS AND WALTER ROWLEY
(From the Laboratory of Physiology of the Northwestern University Medical School, Chicago)

The vasomotor, like the rest of the sympathetic nervous system, is selectively stimulated by epinephrin ("Elliott's Law"). The fact that adrenal gland destruction results in vasomotor failure has often been ascribed to deficiency of circulating epinephrin. The epinephrin has been supposed to exert its influence either (a) by serving as a constant "tonic" stimulant or (b) by facilitating the transmission of impulses from the sympathetic terminals to the smooth muscle cells.

Various investigations have shown that the "tonus theory" is untenable. This report deals with an investigation of the "transmission theory." It attempts to answer the question: Are sympathetic impulses better transmitted in the presence of circulating epinephrin?

In all the experiments dogs have been used. They were anesthetized in various ways,—by ether, urethane-ether, paraldehyde, or by decerebration. Various methods of stimulating the vasomotor apparatus were employed: (a) faradization of the sciatic nerve which reflexly stimulates the vasoconstrictor centers; (b) nicotin injected by vein which stimulates both the centers and the peripheral ganglia; and (c) direct stimulation of peripheral (splanchnic) sympathetic nerve trunks. The reactions to such stimulation were recorded on a kymograph by means of an ordinary mercury manometer connected with a femoral artery. Then through a hypodermic needle in a jugular vein adrenalin in 1:100,000 dilution was slowly infused. While the adrenalin was flowing the stimulation was repeated exactly as before and the result again recorded.

Contrary to expectation it was found that the vasomotor reactions were actually decreased by the epinephrin. The degree of depression varied markedly in different animals, but with possibly one exception all showed it. The rate of infusion was a factor in the results. In some dogs the depression was observed when the rate of infusion was such as to produce no rise or even a fall of general blood pressure. Ordinarily, however, it occurred only when the rate was such as to raise the pressure 30 or more millimeters of mercury. The matter is being further investigated with a view to a subsequent detailed report.

March 8, 1915.

TRAUMATIC LACERATION OF THE ENDOCARDIUM WITH THROMBUS FORMATION IN THE RIGHT AURICLE, RUPTURE OF THE LIVER AND RIGHT ADRENAL, FROM INDIRECT VIOLENCE

J. B. MACLAREN

(From the Pathological Laboratory of Rush Medical College.)

M. R., aged 35, female, and a cook, was admitted to the Cook County Hospital to the service of Drs. Besley and Cubbins because of injuries due to jumping from a third floor while mentally despondent over a supposed illegitimate pregnancy. She had given birth to one illegitimate child four years previously and seven months before had been rendered unconscious in a street car accident, following which there was an alleged mental unsoundness.

Examination revealed a Colles fracture of the left forearm, both bones of the right broken close to the wrist, laceration of the inside of the mouth, and superficial bruises. During the 12 days she lived she passed progressively through a period of mental aberration and restless delirium to one more violent followed by stupor and coma. A gradually rising temperature attained 103° to 107° F. during the terminal 24 hours. The few complaints were of a precordial or more general soreness, headache and nausea; there was no vomiting. The pulse rose gradually to 154° on the ninth day,

dropped to 96° on the following day and from then on was irregular and not easily determined; respiration unchanged until the day before death, then shallow, irregular and accompanied by cyanosis.

Constipation obtained after the second day and was overcome by only the most vigorous cathartics. Except for some blood in the urine, it was not notably altered.

Among the alterations found post mortem (Dr. E. R. LeCount), the following are pertinent to this report: "Traumatic fractures of both forearms at the wrists; healing external bruises and abrasions; healing lacerations of the liver; large traumatic hemorrhage in the lobus Spigelii of the liver; extensive thrombosis of the hepatic veins; large hepatic infarcts; traumatic hemorrhage in the right suprarenal gland; laceration of the lining of the right auricle with thrombus formation; slight pulmonary embolism; disappearing hemopericardium and hemoperitoneum; disappearing traumatic hemorrhages about the thyroid gland, the right kidney, the ascending colon, in the mediastinal and subepicardial tissues and about the crura diaphragmae."

The pulmonary embolism was occlusion simply of a single branch of the third order of the pulmonary artery in one lung by a small clot loosened from that in the right auricle.

Viewed from above; the liver has two tears in the superior capsule which extend transversely in front of the right superior coronary ligament 3 and 3.5 cm. respectively. The posterior tear begins 2 cm. from the right liver border and extends to the left 5 cm. The other tear, 5 mm. in front of this begins near its left end. Both are 2 mm. wide at their widest part, taper to very narrow cracks at either end and are bridged by strands of capsular substance at short intervals.

To the right of the suspensory ligament there is an extensive reddish purple infarct which involves the entire width of the liver at the suspensory ligament and extends to the right in an irregular semi-circle 7.5 cm. This area is neither raised, depressed nor differs in any gross way from the rest of the liver except in color.

The under surface of the viscus has this type of discoloration in the quadrate lobe only. The lobus Spigelii is a deeper red color than the quadrate lobe. The infarcted area is bounded by the fissure of the gall bladder on the right and that of the round ligament on the left. The left, right and caudate lobes are normal.

By cutting the liver sagittally into segments 2.5 cm. thick the ruptures of the capsule are found extending simply through the capsule. The infarcted portion is roughly coni-

cal with the base directed toward the convex liver surface, the apex in the lobus Spigelii. It encompasses a central portal plexus in its right border (Fig. 1). Just to the right of the suspensory ligament the entire liver substance is involved except the caudate lobe (Fig. 2). The infarct is deep red and somewhat softer than normal. All the vessels traversing this region are thrombosed, the larger hepatic veins with well organized mixed thrombi, the smaller, both portal and hepatic, with red thrombi. These extend in the portal vessels to the hilus and in the hepatic to the large vessels which have organized clots and which traverse the lobus Spigelii to the mesial side of the cava.

The entire Spigelian lobe appears to be replaced by blood; it is dark red, friable and soft. From here this hemorrhage

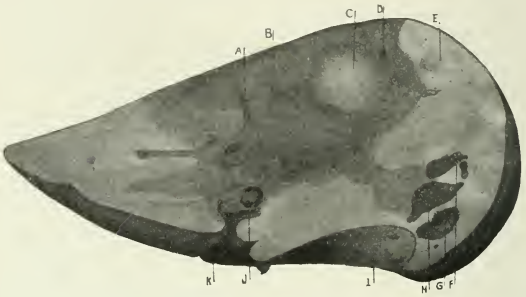

Fig. 1.—Sagittal section through the right edge of the infarct of the liver. *A*, large branches of the portal vein; *B*, infarcted area; *C*, *E*, normal liver substance; *D*, thrombosed hepatic vein; *H*, *F*, hematoma; *G*, *I*, normal hepatic veins; *J*, thrombosed portal veins; *K*, transverse liver fissure.

extends upward, forward and to the right 6 cm. and is about the size of a pullet's egg with the smaller end upward (Figs. 1 and 2). The vessels here are thrombosed and entirely occluded with well organized red thrombi. Grossly none of the vessels show any rupture of its walls.

Beneath the epicardium covering the left auricle about the roots of the pulmonary veins there are three blood clots. Beneath the epicardium covering the right auricle there are extensive subserous hemorrhages especially about the cavae. Within the right auricle, a well organized pedunculated blood clot which measures 3 cm. long by 1.5 cm. wide by 1 cm. thick hangs down from its broad attachment between the

fossa ovalis and the opening of the coronary vein, over the base of the median tricuspid valve, to the right over the Valvulæ Thebesii and partly over the opening of the vena cava inferior. This clot is much more organized at its base than at the periphery and has a general lobulated form (Fig. 3).

Subendocardial hemorrhage is most extensive around the superior cava and base of the auricular appendage. The endocardium itself is torn and lacerated, particularly around the root of the superior cava and opening into the auricular appendage. These extend through to the muscularis, are 1 mm. to 5 cm. long and differ in extent from mere cracks to complete loss of endocardium over considerable areas. Of these last, the greatest is at the opening of the auricular

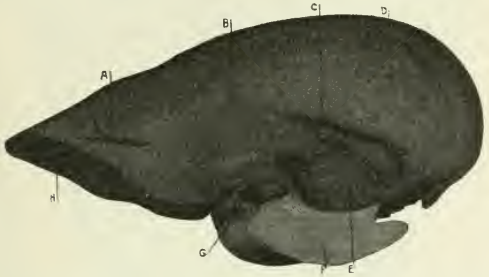

Fig. 2.—Sagittal section to the right of the fissure of the gall bladder through the infarct. *A, D,* thrombosed hepatic veins; *B,* infarcted liver tissue; *C,* thrombosed large hepatic vein; *E,* hematoma; *F,* normal caudate lobe; *G,* portal vessels in hilus; *H,* fossa of gall bladder.

appendage, is an irregular diamond shape, 2 cm. long by 1 wide and is partly covered by a gray organized clot (Fig. 3). No part of the lining of the auricle is entirely exempt from some of the above types of injury. The rest of the heart is normal.

The cortex of the right adrenal posteriorly is lacerated transversely near its center. On cross section (Fig. 4) a large hemorrhage occupying the medullary portion of the gland and entirely replacing it below is exposed. Above this the medulla is pale.

Histology.—Sections prepared for microscopic examination from many places in the liver possess in general the changes to be expected from the gross alterations. The only features

deserving special mention are the extensive necrosis of the liver tissue in the infarcted region which occupies altogether about one-third of the liver and the presence of large

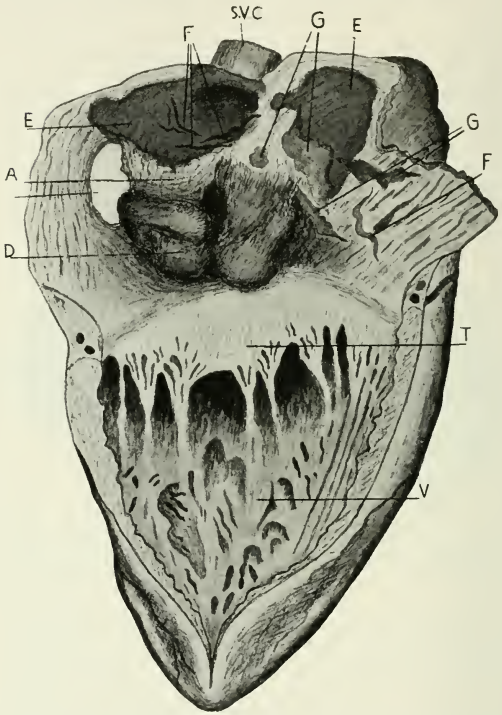

Fig. 3.—Right auricle and ventricle of the heart with trauma and clot. *V*, right ventricle; *T*, tricuspid valve; *A*, right auricle; *S V C*, superior vena cava; *V C*, inferior vena cava; *D*, clot on lateral auricular wall; *E*, subendocardial blood extravasation; *F*, lacerations through endocardium; *G*, areas in which endocardium is missing.

masses of bacteria in the large blood vessels of this dead tissue. The appearances of these masses of bacteria as well

as their absence from the healthy liver tissue and the short time intervening between death and the post-mortem examination altogether support an assumption that their proliferation when found was at least in large part ante mortem.

Simultaneous injuries such as these of the liver and heart and adrenal and caused by injuries of a non-penetrating character are very rare. In the most extensive review of trauma of the liver, I have been able to find that of Amante[1] of more than 1,000 cases there is no reference to accompanying injuries to the heart. Thöle[2] found 73 of 188 injuries of the liver associated with injuries to other organs, but in none of these was the heart or adrenal included. Those

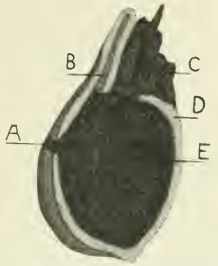

Fig. 4.—Cross section of the right adrenal. *A*, rupture in cortex; *B*, medullary portion; *C*, plexus of vessels; *D*, cortex; *E*, hematoma into medulla.

most frequently injured according to Thöle are the right kidney (27) and the spleen (18). Sherk[3] found the liver involved in 22 of 293 subcutaneous (non-penetrating wounds) injuries of abdominal viscera, none with accompanying injury of the adrenal. Geill, cited by Thöle, loc. cit., places the incidence of subcutaneous liver rupture alone at 59.9 per cent. and in the experience of Edler, cited by both Thöle and Amante, non-exposed liver injury was met 189 times and injury to other organs 176 times in 365 cases.

1. LeLesioni Traumatiche del Fegato e delle Vie Biliari, Rome, 1912.
3. Jour. A. M. A., 1911, 56, p. 179.
3. Jour. Am. Med. Assn., 1911, 56, p. 179.

With regard to trauma of the heart not caused by penetrating wounds Reidinger[4] found 34 in 452 cases of trauma of all sorts and of these 34, 28 were apparently due to direct violence since they were associated with fractured ribs or sternum or both and in all the right auricle was involved; only once was the injury due to falling from a height. Fischer[5] was able to find only 20 reported injuries of the heart resulting from falls from varying heights. According to Hirschfelder,[6] Bernstein in 1896 collected 126 cases from the literature dealing with non-perforating injuries of the heart and of these 42 came to post-mortem examination; the endocardium alone injured in 16, the visceral pericardium alone in 10, pericardium and myocardium in 5, the endo- and pericardium in 5, endo- and myocardium in 4. In this connection reference may be made to the experiments of Külbs[7] who produced traumatic hemorrhage in the heart valves of dogs by blows on the left thorax.

Traumatic hemorrhage in the suprarenal glands is not rare and is especially common from efforts to resuscitate newly born infants by the Schultze method.

Subcutaneous injuries of the liver may consist of (1) rupture of the capsule with the underlying parenchyma, (2) rupture of the parenchyma alone with the extravasation of blood into the space so formed, (3) small multiple ruptures with resulting multiple hematomas (liver apoplexies). The first may be only slight or consist of the total avulsion of a lobe. The second may be of any degree to the complete pulping of the liver. The injury I have described is of the second type; the rupture in the capsule does not extend into the parenchyma, while the chief injury is laceration of the Spigelian lobe.

The mechanism of liver rupture is of three types; direct blows over the liver either against the costal margin or abdominal parietes produce subcapsular rupture opposite the point of impact (percussion); excessive bending or flattening of the liver (compres-

4. Deutsche Chirurgie, 1888, 42, p. 178-182.
5. Arch. f. clin. Chirurgie, 1868, 9, p. 571.
6. Diseases of the Heart and Aorta, 1913, p. 617.
7. Verhandl. d. dent. path. Gesellsch., 1908, 12, p. 172.

sion) with rupture of the superior or inferior capsule; indirect injuries (contra coup or concussion) from the sudden propulsion of the liver in any direction and a like sudden arrest of it by its ligaments or by striking the diaphragm, back-bone or parietes and produced most frequently by falls.

As regards the injuries I have studied, the patient probably struck the ground in a semi-prone position with the arms thrown backward which is shown by the bruised feet, fractured arms, torn buccal mucosa and absence of other external injury. In such a position the liver would be thrown downward against the slightly resistant intestines, but because of the fixation of the diaphragm and resistance of the suspensory and coronary ligaments bent most in its anterior lateral portions with compression of the Spigelian lobe and caval fissure between the bulk of the liver and the vertebrae. Infarction is secondary to thrombosis and hemorrhage, the results of injury to the hepatic veins, and the natural slowness of the blood flow in them. The portal veins and hepatic artery continued to supply the blood to the region drained by the thrombosed hepatic veins and in turn became thrombosed when the tissues were saturated and the onward blood flow arrested in them.

Ellis[8] states that adrenal hemorrhage results most frequently from thrombosis of the adrenal veins. In the case I have described there was no involvement of the adrenal veins. Theoretically the injury might result from two conjoined forces; the sudden compression of the vena cava by the descent of the liver with momentary back pressure in the adrenal and at the same instant the direct adrenal compression between the liver and the lower ribs serving to rupture the delicate and thin capillaries of the medulla. The same pressure caused the rupture of the cortex.

Rupture of the right auricle or its endocardium usually results from fracture of the ribs or sternum. In this case, there was no such fracture and the mechanism is problematical. Sudden downward thrust of the heart while the diaphragm is in descent, the auricle

8. Cleveland Med. Jour., 1912, 11, p. 1-80.

distended with blood and the ventricle contracted at the prediastolic period might exert sufficient traction on the superior auriculo-caval junction to cause endocardial laceration with secondary subendocardial and subepicardial extravasation and secondary thrombosis on the rough surfaces of the rents. To this mechanism should be added increased blood pressure in the auricle incident to the caval compression occurring at the same instant as the downward thrust.

The prognosis in a complicated injury of the heart, liver and adrenal is grave. Individually the prognosis varies with the organ injured. Faure and Labey[9] have noted that aside from the danger of death from hemorrhage, the non-infected injured liver tissue may either become absorbed and the hepatic tissue regenerate or cicatrize, encapsulate or encyst spontaneously without symptoms. Abscess, with the associated phenomena and prognosis of pyogenic subphrenic abscess, follows in infected cases.

Injury to the adrenal is always of grave significance and though doubt is cast by recent investigators on the significance of the adrenal medulla in the body economy, hemorrhage into it leads almost without exception to death. Against this, Tom A. Williams[10] maintains that the medulla is not essential to life and quotes Karakascheff who examined a child, 5 to 6 months old, after death, in which the adrenal cortex was intact but the medulla destroyed on both sides by hemorrhage so long before that calcification had taken place. Hoskins[11] says, "On the whole, it seems most likely that the characteristic asthenia of adrenal deficiency is due to the loss of cortical tissue, whereas the medullary part has as its chief function the furnishing of a special stimulant to enable the body to cope with emergencies." The lack of this special stimulant, epinephrin, in injuries with medullary hemorrhage is undoubtedly the cause of death.

According to Reidinger, ventricular injuries of the heart often heal spontaneously while trauma to the

9. Noveau Traite de Chirurgie, Paris, 1910, 27, p. 3-5.
10. Jour. A. M. A., 1914, 63, 2206.
11. Jour. A. M. A., 1914, 62, 1805.

auricle of any sort is 86 per cent. fatal, usually from hemorrhage into the pericardium.

In conclusion, I wish to refer again to the exceptionally long time, twelve days, intervening between the accident and death and to the absence of noteworthy symptoms accompanying the gradual failure and approaching death; this last feature was of especial interest to Drs. Besely and Cubbins, to whose courtesy I am obliged for the opportunity to make this report.

The works of Amante, Thöle, Faure and Labey and that of Reidinger, references to which have been cited, have been freely consulted.

March 8, 1915.

DEMONSTRATION OF SPECIMENS OF PACHYMENINGITIS HEMORRHAGICA INTERNA

EUGENIO FERNÁNDEZ

(From the Pathological Department of Rush Medical College)

Case 1.—At the post-mortem examination of the body of a man who was found unconscious at the foot of a stairway, brought to the Cook County Hospital by the police, and who died an hour later, small superficial abrasions on the right cheekbone and eyebrow were noticed, but no other bruises. "The skull is unbroken. The right side of the dura in front is fluctuant as is also the left. When the dura is sectioned on the left side a large amount of blood escapes, especially behind. Underneath the dura there is clotted blood in considerable amounts. There are no changes in the dural sinuses. The compression of the front end of the brain is very marked. There is also fluid blood in the anterior fossae. The inner surface of the dura is covered with a brown layer of fibrin on each side, most marked on the left. The clotted and fluid blood in the subdural space weighs 145 gm. Little else of interest is found in the other organs of the body aside from sclerosis of the basilar artery, slight hypertrophy of the left ventricle; myeloid metaplasia of the diploë of the bones of the skull; cloudy swelling of the liver; passive hyperemia and cloudy swelling of the kidneys; healed, calcified and encapsulated tuberculosis of the lungs; and right obliterative fibrous pleuritis."

After hardening the brain and its membranes the following record was made: "The dura over the right temporoparietal region has an oval shaped elevation 9 cm. anteroposteriorly and 4.5 cm. coronally because of a fresh blood clot encapsulated between two definite layers of this membrane. The upper layer is thick and resistant, the lower thin and less firm. At the border where they meet there is no visible line of cleavage. Their lining is apparently continuous. This border is thicker than the adjoining dura and contains six small openings which lead between the two layers but which cannot be traced as definite blood vessels. Elsewhere the dura appears normal. The brain is small and of irregular contour. Over the right hemisphere there is a concavity shaped anteroposteriorly like a small stream-bed. Its floor consists of flattened convolutions and almost obliterated sulci; and its mesial bank of a ridge of brain substance sloping upward to the longitudinal fissure. Its outer border is less elevated and continues with the sloping downward vertex. It begins 2 cm. caudad of the frontal pole and extends posteriorly 14 cm. Coronally it measures 4.5 cm. and begins 2 cm. from the longitudinal fissure. The ventral surface of both frontal lobes is decidedly cupped, averaging about 1 cm. in depth. There are no other changes except that the basilar artery has a small, discrete, yellowish-gray thickening about 1 mm. in diameter in its wall. The lateral ventricles are about one-half their normal width, the right narrower than the left."

Microscopic.—The blood dissected the dura into two definite laminae, a thick upper membrane made up of four layers and a thin lower membrane which has only one, the visceral layer of the dura composed mostly of elastic longitudinal fibers and cells with large round and oval nuclei. The four layers of the outer membrane are the vascular periosteal layer made up of cells with large round or oval nuclei—osteoblasts—embedded in abundant loose interstitial tissue; two compact fibrous layers; and the fourth an irregularly torn, wide layer, largely made up of a few fibrous connective tissue cells with few nuclei, numerous capillaries running at right angles to the axis of the fibrous tissue, fibrin deposits and extravasated blood cells.

Case 2.—After drinking continuously for several weeks, P. G., aged 30 years, a white man, was taken to the Hospital of the House of Correction. He died there after 17 days during which he was irrational and paralyzed on one side.

Anatomic Diagnosis. — Pachymeningitis hemorrhagica interna; great compression of the left cerebral hemisphere;

external healing abrasions; disappearing bruises of the scalp; marked emaciation; marked edema of the lungs with hypostatic bronchopneumonia; single gummatous (?) scar of the liver.

After hardening the brain it is found that the dura mater has a dark elevation covering the whole left cerebral hemisphere. It consists of a dark brown pseudomembrane (14 cm. by 8 cm. by 1 mm.) encapsulated between the two layers of the dura, an outer thick and resistant and an inner thin and papery. The lepto-meninges are of normal thickness, lustre, and transparency throughout. The subpial vessels and the vessels at the base of the brain are engorged with blood. The brain is decidedly asymmetrical, the left hemisphere from 2 to 5 cm. shorter than the right because of a trough-like concavity just under the affected portion of the dura. The left lateral ventricle has completely disappeared and the right is reduced to about one-half its normal size.

The microscopic changes are very similar to those already described, except that at the point of meeting of the two laminae into which the blood dissected the dura, the torn, vascular layer is about twice wider than the other layers combined. Its blood vessels are markedly dilated. There are a few fibrin deposits, and little infiltration of blood cells, but numerous small deposits of blood pigments are scattered throughout. Nowhere is there evidence of tissue reaction.

Case 3.—At a post-mortem examination made by Dr. Wells in 1905 on the body of a negro, aged 40, brought unconscious to the Cook County Hospital and who died shortly after, no external injuries were found.

"The calvarium is very thick, and when the dura is opened in the left side a considerable amount of brownish turbid fluid escapes. This fluid is entirely subdural. There are no changes between the dura and the skull. On the under surface of the dura on the left side is a brownish red rather firm mass from 2 to 5 mm. thick, looking like an old disorganized blood clot. It is firmly attached to the dura, forming a complete uniform layer and has a sort of membrane on its visceral surface. This covers the dura from the median line above to the sphenoid below and over the anterior two-thirds of the cerebral hemispheres. The left side of the cerebrum is flattened over to the right, and over the anterior portion this reduces the size of the brain from 4 to 6 cm. in thickness. There are also a few small clots attached to the internal surface of the dura on the right side. The veins of the meninges are greatly engorged. The basal ganglia and lateral ventricles are not changed. The arteries

at the base of the brain show some sclerotic patches. The brain substance appears to be normal throughout. There is no fracture of the skull. It is impossible to find the source of the hemorrhage. Beginning at the foramen spinosum on the left side and extending up the division of the middle meningeal artery is an extensive erosion of the bones of the skull 5 to 6 mm. wide. The artery and its two branches are surrounded by a soft pink mass of granulation tissue exactly corresponding to the eroded area. The artery is tortuous during this part of its course and contains numerous sclerotic patches but its lumen is not enlarged at any point."

There is also a beginning hypostatic bronchopneumonia, a gumma of the spleen, and sclerosis of the coronary arteries.

"Microscopically, the dura is thickened. This is due to the formation on its visceral surface of a thick layer of granulation tissue. Near the dura proper this membrane is older, as shown by the adult character of the connective tissue and the absence of blood vessels. In this newly formed membrane are a few areas of extravasated blood and much blood pigment, showing the existence of previous hemorrhages. There is much increase in the elastic tissue throughout the dura mater and especially the limiting membranes are very pronounced. There are a few calcified areas in the granulation (old) tissue. The tissue around the branches of the meningeal artery is typical granulation tissue."

Case 4.—F. S., a white man, aged 50, was arrested for alcoholism and taken in a semi-rational state to the Hospital of the House of Correction with a temperature of 104, pulse 100, respirations 26. He was unable to control his rectal and vesical sphincters. He had no ataxia, no tremors, and all the reflexes were present, but sluggish. He was able to walk unassisted. He developed later bronchopneumonia. The spinal fluid contained two lymphocytes per mm.[3] The Nonne was negative. A clinical diagnosis of delirium tremens and pneumonia was made.

Post-mortem examination by Dr. LeCount revealed the following five injuries on the external surface of the body: "(1) Healing abrasion over the back of the left wrist 1 x 1.5 cm.; (2) purplish red discolorations about the backs of both elbows: (3) seven small purplish bruises of the left upper arm; (4) a greenish yellow bruise in the tissues in the anterior fold of the right axilla, 2.5 x 3 cm.; (5) over the lateral surface of the right lower leg, a linear abrasion 2.2 cm. long. There are no injuries in the pericranial tissues except two small purplish bruises on the right side, 1 and 2 cm. in diameter, respectively." Search for a fracture of

the skull was quite thorough. "There are no injuries on the outside of the dura." It is very tense especially on the left side. On removing it from the brain there is found a region of thickening on the left side, which is apparently in the dura itself, and which has compressed markedly the cerebral hemisphere. There is an abundant amount of blood-stained cerebrospinal fluid. In the region of the right sphenoparietal suture is a reddish yellow thin material between the dura and the skull. It can be easily removed. There are no signs of fracture here nor are there any injuries in the temporal muscle opposite this region. The skull bones are thin and there are numerous purplish discolorations in the vault and base.

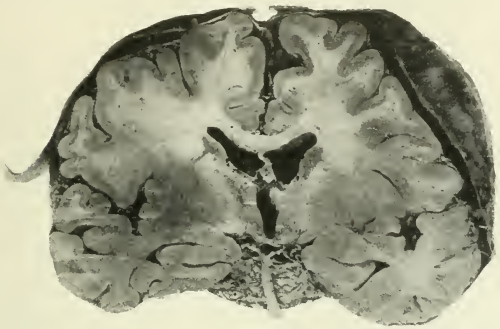

Fig. 2.—Case 4. Illustrating the blood clot between two layers of the dura on the left side of the brain and the compressed brain.

There are no other changes of interest in the rest of the body except traumatic subperitoneal hemorrhages of the ascending colon; marked passive hyperemia of the lungs—hypostasis—with bronchopneumonia; marked cloudy swelling of the liver and kidneys with some fatty changes; myeloid diploë.

After hardening the brain the dura over the left side remains tense, elevated and hard because of an oblong mass practically covering the whole hemisphere (Fig. 1). This mass is 14.5 cm. anteroposteriorly, 9.5 cm. transversely, and 1.5 cm. in thickness and is composed of irregular layers of a gelatinous material simulating peculiar arabesques of varied coloring, some yellow and separated from the others by a bluish gray homogeneous substance, others dark brown, still

others dark blue. It is definitely encapsulated by two layers of dura, the outer 1.8 mm. thick, the inner about 1 mm. The dura is adherent to the lepto-meninges by thick fibrous adhesions over the ventral surface of the left temporal lobe. The meningeal vessels are prominent. The pia is milky and thickened over the same region but of normal transparency, lustre and thickness elsewhere.

The subpial vessels are distinctly engorged with blood. Those at the base of the brain stand out prominently though empty. The convolutions just under the masses are flattened, forming a straight line instead of describing an arc with its convexity outward. Those corresponding to the motor areas are prominent and narrow, the sulci deep and opened. The ventricles are dilated, especially the anterior halves of the two lateral ones and the posterior portion of the third.

Microscopically the growth has a thick, fibrous, compact pseudocapsule and consists largely of a homogeneous, acid-staining undifferentiated substance. Fibrin strands arranged in small clumps, young fibrous connective tissue invading from the periphery, greenish yellow deposits of blood pigments, and fresh hemorrhage give this homogeneous background a varied appearance. The degenerating blood cells form a coarsely or finely granular débris wherever found. There is present also a small number of thin walled capillaries.

Of the two theories most widely discussed by writers on pachymeningitis hemorrhagica interna, the inflammatory and the hemorrhagic, the evidence obtained from the study of these four cases seems to support the latter. Also although the clinical data is very meager, that obtained, aside perhaps from the luetic splenitis of the negro, points to alcoholism as a prominent etiologic factor.

March 8, 1915.

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CONCERNING PROTEOLYTIC FERMENTS IN PORTAL BLOOD

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Abderhalden gives as his reason why blood must not be taken shortly after meal time, when performing his test for the serodiagnosis of pregnancy and other conditions, that the blood at this time contains an increased amount of amino-acids and a positive reaction may result from the dialysis of these without there having been ferment activity going on in the test.

The writer believes that this explanation will not hold because when inactivated serum and placenta was used as a control no dialization occurred even when the blood was taken from men and dogs at the height of digestion. He attempts to explain this theoretically on the ground that it is probable that ferments are absorbed from the gastro-intestinal tract during digestion thus increasing the ferment content of the blood, which thereupon has the power of proteolytic cleavage.

To gain some evidence regarding this conception, blood was taken from the peripheral (femoral) and portal (mesenteric) circulations of dogs, some of which were in the fasting state and others at the height of digestion.

It was shown that the portal blood was richer in ferments at the height of digestion than the femoral blood, although positive reactions resulted in each case.

In the fasting state, on the other hand, the reactions were weak in the portal bloods and absent in the femoral blood. The explanation of the positive reaction in the portal blood in the fasting dogs is that there is normally a secretion of pancreatic juice thrown into the bowel about every two hours in the dog even when fasting (Boldireff).

It is suggested that a possible explanation of the stronger reaction in the portal blood is the fact that the majority of the fat and lipoidal substances are thrown into the blood through the throacic duct. Jobling and Petersen have shown that these are the substances that inhibit the action of trypsin and leucoprotease. Hence the portal blood might be expected to show more tryptic activity because of the relative paucity of antitrypsin.

The whole experiment seems to point to the fact that there is in all probability a remarkable conservation of ferment in the body economy, through absorption from the gastro-intestinal tract in this way. It is suggested that it is possible that the pancreas and digestive glands might in this way be the chief supply of the diffusible or extracellular ferments of the body. It is also probable that the liver ferments are supplied and replenished continuously from this source.

CONCLUSIONS

1. The portal and the peripheral blood in the dog contain a demonstrable increase in the amount of proteolytic ferment at the height of digestion.

2. This is also true of the portal blood of the dog in the fasting state.

3. Under both the above conditions the portal blood is relatively richer in ferment than the peripheral blood.

4. The probable source of this ferment is the ferment-rich contents of the intestinal canal at the height of digestion.

April 12, 1915.

COMPLEMENT FIXATION IN THE DIAGNOSIS OF GONOCOCCAL INFECTIONS

ERNEST E. IRONS
AND
H. K. NICOLL

SUMMARY

A strong or moderate positive reaction obtained with adequate technical controls indicates the presence or recent existence of gonococcal infection.

A weak positive reaction has only a limited confirmatory value, and if the test is being made for diagnosis it should be repeated.

The reaction may change from positive to negative and from negative to positive during the course of an infection. This possibility should be taken into consideration in the interpretation of a negative result in a suspected case.

The reaction may become negative while gonococci are still present in the body and so a single negative reaction must be interpreted with great caution either in the diagnosis of infection or the determination of cure.

April 12, 1915.

THREE INTERESTING CASES OF LUES

W. H. BURMEISTER

Case 1.—The patient, a white man about 50 years old, was found in his room in a comatose condition. He was taken to the Cook County Hospital.

Briefly, at that time he was having tonic and clonic spasms, which were more marked on the right side. No paralysis. Neck not rigid. Eye grounds negative. Thorax and abdomen negative. Pulse rate 120; blood pressure 175 mm. Reflexes present except cremasteric and abdominal. Knee jerks slightly increased, neck later became rigid. Double Kernig. Head constantly turned to left. Eyes turned to the right. No nystagmus. Right pupil slightly larger than left. Both pupils react to light. Leukocytes, 38,500; Hemoglobin, 88 per cent. (Dare). Urine: Albumen, ++; granular casts and erythrocytes. Spinal puncture: 8 c.c., clear; erythrocytes, few lymphocytes; Noguchi, +.

Anatomic Diagnosis: Leptomeningitis; multiple gummas of the scalp and skull; sclerosis of the coronary arteries and aorta; sclerosis of the basilar vessels; marked atrophy of both the frontal lobes of the cerebral cortex; marked fatty changes and passive hyperemia of the liver; passive hyperemia and cloudy swelling of the kidneys; cloudy swelling of the myocardium; "black and blue" right eye; linear wound over the right orbit; laceration and discoloration of the skin of the chin; superficial healing abrasions of the skin of the extremities; hyperplasia of the spleen; marked hypostatic hyperemia and edema of both lungs; passive hyperemia of the trachea and main bronchi; catarrhal tracheitis and bronchitis; fibrous patch of the epicardium; fibrous obliterative pleuritis; healed scar in the apex of the left lung; marked marginal emphysema of both lungs; small papillomata of the skin of the lower anterior abdominal wall; fetal lobation of the kidneys; pyorrhea alveolaris.

SPECIMEN DEMONSTRATED

A number of more or less circular regions of gummatous infiltration are found in the pericranial tissue. These are yellowish gray and have a somewhat pearly appearance at the borders. In all cases they are a part of a similar process found in the bone of the underlying skull. In the right temporal bone there is a gumma involving all portions of the bone over an area roughly circular in outline and 4 cm. in diameter. This gumma has infiltrated the underlying dura and involved the leptomeninges beneath it over an area about 1 cm. in diameter. In the parietal bones bordering the sagittal suture there are two similar more or less circular gummatous infiltrations 6 to 7 cm. in diameter. These also involve the overlying periosteum and the underlying dura. The dura over the convexities of both cerebral hemispheres presents a gummatous pachymeningitis and an acute hemorrhagic pachymeningitis interna. The gummata in the dura are close together, grouped close to the superior longitudinal sinus and vary in size from nodules the size of a pea to that of a large Lima bean. In some of the underlying leptomeninges there is a secondary infiltration at their points of contact with the overlying larger local gumma. In the leptomeninges, scattered irregularly over the convexities and usually at the bifurcation of the blood vessels or close to the side of a larger vessel there are a considerable number of opaque thickenings which have a pearly gray appearance. None of these measure more than 1 to 2 mm. in their widest dimensions. There is a marked edema of the leptomeninges and considerable hypere-

mia of them. There is a marked atrophy of the convolutions of the frontal lobes of the cerebral cortices. The basilar vessels present only a few very minute thickenings. There are no gross changes on the surface of a section of the cervical cord in the regions of Goll and Burdach. There are no gross changes on the base of the brain or in the dura covering the base of the skull. There are no gross changes on the surfaces of sections of the optic nerves.

Case 2.—White infant, girl, 18 months old. No history obtainable except that child had accidentally inhaled considerable coal gas two days prior to death. "There were no symptoms of illness, however, at any time." The child was found dead in bed. The trunk cavities only were opened. Anatomic diagnosis: Edema of the lungs; acute catarrhal bronchitis; hyperplasia of thymus; parenchymatous degeneration of myocardium and kidneys; chronic splenic tumor; interstitial luetic hepatitis with miliary gummata; postmortem malacia of pancreas and adrenal glands; general anemia.

SPECIMEN DEMONSTRATED

The liver is large, firm, and has a relatively sharp edge. Its capsule is smooth and glistening. The liver is a light brick yellow in color. On section no definite acinus structure can be seen. Very little blood can be expressed from the cut surface. Scattered throughout the liver are numerous pinpoint-sized, grayish opaque-appearing circular areas. As many as 4 to 6 of these can be seen in a square cm. of area.

Microscopically the liver presents a diffuse interstitial hepatitis consisting in diffuse loosely arranged fibrillae and newly formed spindle cells. The arrangement of liver cells in cords is no longer evident. Scattered throughout the section and also arranged in small groups are seen cellular infiltrations consisting for the most part of lymphoid cells; cells with small deeply stained, sharply outlined nuclei. Frequently the centers of these cell groups have undergone necrosis, the necrotic material being homogeneous in appearance and containing considerable blue (hematoxylin) staining nuclear débris.

Levaditi stains are positive for spirochetes, which, however, are not very numerous. Stains for tubercle bacilli are negative.

Microscopic examination of spleen, kidney, pancreas, myocardium and lungs shows these organs to have a slight interstitial new formation of connective tissue and diffusely scattered lymphoid cells. Levaditi stains are negative.

Chemical and spectroscopic examination of blood reveals no trace of carbon monoxid.

Case 3.—White man, aged 30 years. No history of illness obtainable; found dead in workshop.

Anatomic diagnosis; edema of lower extremities; small fibrous scar apex left lung with partial obliterative fibrous pleuritis on same side; marked emphysema and anthracosis. Excentric hypertrophy of both ventricles of heart. Non-obliterative fibrous epicarditis right ventricle; multiple confluent gummata of myocardium. Moderate atherosclerosis of aorta; slight sclerosis of coronary arteries. Chronic passive hyperemia of liver, spleen, and kidneys.

SPECIMEN DEMONSTRATED

The pericardial sac contained about 10 c.c. of clear, colorless fluid. The heart was large and relatively flabby in its consistency. There was an excentric hypertrophy of both ventricles. The right ventricle wall measured 10 mm. in thickness, the left 19 mm., despite a marked dilatation in both instances. The myocardium was a pale brown in color and quite friable. In the upper lateral portion of the wall of the right ventricle are seen on section ten or twelve partly confluent grayish nodules measuring 1 to 3 mm. in diameter. These nodules occupy an area roughly 4 to 5 cm. in extent. Throughout the myocardium of this area between the nonconfluent nodules the muscle has a paler grayish somewhat opaque appearance. The valvular and mural endocardium is without noteworthy gross change.

Microscopically a marked perivascular infiltration of lymphoid cells is present in both right and left ventricles and septum. In that portion in which the changes are evident on gross inspection typical gummata are present with relatively numerous giant cells and a very marked diffuse connective tissue and lymphoid cell infiltration.

Levaditi stains reveal the presence of spirochetes in moderate numbers.

April 12, 1915.

THE EFFECT OF BENZENE ON THE PRODUCTION OF ANTIBODIES

LUDVIG HEKTOEN

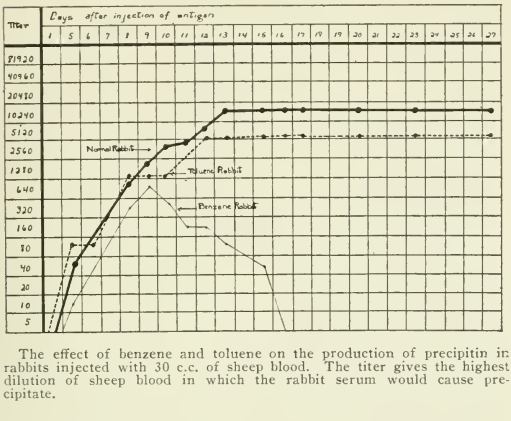
(From the Memorial Institute for Infectious Diseases, Chicago)

From the investigations of Selling[1] we know that in rabbits, at least, benzene in suitable doses produces a profound destruction in the hemopoietic organs, especially the bone marrow, followed, when recovery

1. Zeigler's Beitr., 1911, li, 567.

takes place, by regeneration. During the height of this effect on the blood-making organs, there is a great diminution in the number of leukocytes in the circulating blood, the granular forms being relatively more involved than the lymphocytes. Of changes in other organs produced under these circumstances, may be mentioned fatty changes in the liver and kidneys and hemorrhages in the walls of the stomach, the intestines, and in the lungs and in the pleura.

The toxic effects of benzene on the leukocytes and on the leukopoietic organs are now being utilized in



The effect of benzene and toluene on the production of precipitin in rabbits injected with 30 c.c. of sheep blood. The titer gives the highest dilution of sheep blood in which the rabbit serum would cause precipitate.

the treatment of leukemia, but so far without any permanent curative effect.

In view of this action of benzene, it lies near at hand to test its effects on the production of antibodies, because a number of facts indicate that the blood-making organs are concerned very largely in their manufacture. The observations of Pfeiffer and Marx and others show that certain antibodies can be demonstrated in the bone marrow, spleen, and lymph glands before they can be demonstrated in the blood; under certain circumstances the removal of the spleen

diminishes the amount of antibody produced; when the blood-making organs are stimulated, as in acute anemia, the production of antibodies is increased; when the blood-making tissues are destroyed, as by Roentgen ray, the production of antibody is diminished; and finally, it has been shown recently by Carrell and Ingebretson and others that in the presence of antigenic substances, cultures of the spleen and bone marrow outside of the body may manufacture antibodies.

Rusk[2] has reported that in rabbits the injection of benzene greatly reduces the formation of lysin for sheep corpuscles and of precipitin for horse serum.

In the experiments now reported, the effects of benzene, C_6H_6 and toluene $C_6H_5CH_3$, on the formation of antibodies in rabbits and dogs have been studied. Merck's preparations were used and the daily amount varied from 0.5 to 1 c.c. per kilo of rabbit, injected subcutaneously mixed with an equal amount of olive oil. It appears that as soon as benzene causes a definite diminution in the number of the leukocytes in the circulating blood in rabbits, there results also a distinct inhibition of the formation of antibodies (lysin and precipitin). In some animals almost no new antibody is produced. Occasionally animals are found which appear to be resistant to the leukotoxic action of benzene, and in such animals there is no inhibition of antibody formation. Toluene, which is without any marked leukotoxic effect, has comparatively much less effect than benzene on the production of lysin and precipitin in rabbits. Indeed, in some animals the injection of toluene may lead to marked prolongation of the production of antibodies, especially precipitin.

In dogs it is difficult to produce leukopenia with benzene, which, in doses of 0.2 c.c. per kilo of the weight of the dog, causes a marked leukocytosis, as well as some increase in the red corpuscles and a distinct increase in the amount of lysin for goat corpuscles.

2. Univ. Calif. Pub. in Path., 1914, ii, 139.

The results obtained, which will be described more extensively elsewhere, confirm the results obtained by Rusk and establish that we have in benzene a substance which in addition to its destructive effect on the hemopoietic tissues, also profoundly affects the production of antibodies, and in toluene a substance that under certain circumstances prolongs the period of antibody production.

May 10, 1915.

REPORT OF A CASE OF CENTRAL AND PERIPHERAL NEUROFIBROMATOSIS

PETER BASSOE AND FRANK NUZUM

The case here reported is of interest not only as a typical example of central and peripheral neurofibromatosis, many of which are on record, but also on account of certain infrequent microscopic changes in the cerebral hemispheres. Among these are regions of calcification, of perivascular connective tissue proliferation and of irregular and isolated cell heaps. These heaps, composed of polymorphous, vesiculated cells devoid of processes recall the condition described by Bourneville as tuberous sclerosis.

Clinical History.—The patient, a boy aged 15 years, was first seen by one of us (Dr. Bassoe) in consultation with Dr. W. A. Phillips of Evanston, Ill., March 23, 1914. The parents and their three other children are well. The maternal grandmother is said to have had a lump on the head and a maternal uncle has a small nodule on the forehead, but enough facts could not be determined to learn whether these really were cases of molluscum fibrosum.

The boy had typhoid (?) fever in 1902 and measles in 1903. The first evidence of his nervous disease was in 1904, when at the age of 5 years he had an attack of pain in the right scapular region suspected of being of the nature of pleurisy, but it was followed by a dragging of the left foot. From that time on he had similar attacks of pain in the right scapular region lasting from two weeks to three months and occurring about once a year. In 1909, eight eye muscle operations were performed for the relief of strabismus. A lump on the left side of the neck was noted at least three years before death, others more recently, while a large mass

attached to the rectum had been discovered only a few weeks before our examination.

The final attack of illness began Dec. 20, 1913, like the previous ones, with pain beneath the right scapula, which lasted for about two weeks and was followed by pain in the left side of the abdomen, difficulty in emptying the bladder, and progressive pain and weakness in the left leg. On account of the scoliosis Roentgen-ray examination of the spine was made and was negative. About March 1 occasional choking when eating set in and the pulse rate became accelerated, being usually above 100. The boy was bright and showed no mental abnormality at any time.

Examination.—March 23, 1914. The boy is very emaciated and exhausted and cannot talk above a whisper. Subcutaneous, movable nodules are seen on the left side of the forehead, on the left side of the neck and on the chest. There is a well-marked dorsolumbar scoliosis with convexity to the right. The patient cannot raise his head from the pillow and the left leg is very weak. Passive movements of the lower extremities are painful. Smell and taste are normal and there is no important visual defect. The right external rectus is weak and the patient sees double when looking to the left. The corneal reflexes are absent and there is distinct paresis of both divisions of the left facial nerve. Hearing is much impaired in the left ear but is normal in the right ear. Ophthalmoscopic examination is negative. The left knee jerk is absent and the right one weak. The ankle jerks and the cremasteric and abdominal reflexes are absent. The Babinski sign is present on the right side, while the left plantar reflex is normal. Tactile sensation is normal, but pain and temperature senses are diminished on the anterior aspect of the left leg and in areas on the abdomen.

The patient gradually grew weaker and the choking attacks became more frequent. By the end of April there was evidence of facial nerve weakness on both sides, as both eyes remained open.

The patient died May 25, 1914.

The necropsy was held twelve hours after death, by the writers.

Anatomic Diagnosis.—Multiple central and peripheral neurofibromata. Marked emaciation. Hypostatic congestion of the lungs. Passive hyperemia of the linings of the alimentary tract, urinary bladder and of the liver and spleen. Slight fatty changes in the kidneys. Accessory lobe of the left lung. Deep sacral decubitus. Inequality of the pupils.

This is the body of a very emaciated white boy, 150 cm. long, and weighing approximately 85 pounds. The head is well covered with long, wavy, brown-black hair. The eyeballs are sunken. The eyes are blue and the pupils are dilated, the right more so than the left. There is no strabismus. The face is smooth and there are no evidences of a beard or mustache. The lips are pale and anemic. The teeth are all present, clean and in good condition.

On the left side of the forehead there is a flattened, irregular, oval, freely movable subcutaneous nodule, 1.5 by 0.5 cm., the long axis parallel with the long axis of the body.

Just above the middle of the left clavicle, in the supraclavicular space, is another firm, somewhat movable nodule, 2 by 1 cm., which is not adherent to the skin.

Over the fourth intercostal space, just to the right of the sternum, is a brownish pigmented, slightly elevated annular area in the skin which is 2 cm. in diameter. In the same interspace and just beneath the nipple is a semicircular, movable subcutaneous nodule. Over the eighth rib in the right midclavicular line is another oval, subcutaneous, firm nodule 1 by 0.8 cm. There are two similar nodules in the fifth interspace in the left anterior axillary line, the larger of which is 2 by 2 cm., the smaller 0.5 cm. in diameter.

Over the sacrum is a circular region of pressure necrosis 3.8 cm. in diameter and extending down to the fascia covering the sacrum.

There is a moderate scoliosis of the lower dorsal and lumbar portions of the spine, the convexity to the right, the deviation being 3.5 cm. from the mid line of the body.

The testicles are in the scrotum and are equal in size. There are no scars on the penis.

The skeletal musculature is markedly atrophied. There are no evidences of injury, either recent or old, on the external surface of the body.

On opening the body the panniculus in the mid line is trifling in amount. The abdominal viscera are normal in size and in their relation to each other. The foramen of Winslow is patent. The urinary bladder is empty and contracted. There is no free fluid in the pleural cavities. There are no adhesions in either the pleural or abdominal cavities.

The lungs are of normal size. There is a small accessory lobe on the upper lobe of the left lung. The pleura is everywhere smooth and glistening. On sectioning the lungs a moderate hypostatic congestion is demonstrable in each lung, the pleura over these regions being darker than elsewhere. There are no further changes in the lungs other than those recorded in the anatomic diagnosis.

There is about 50 c.c. of clear serum in the pericardial sac. The heart weighs approximately 240 gm. The apex is made up of the left ventricle. The epicardium is smooth and glistening, as is the endocardium. The myocardium is in rigor mortis. There are no thickenings or other alterations of any of the valve leaflets. The foramen ovale is closed. There are no subendocardial hemorrhages.

On sectioning the myocardium and the papillary muscles no gross changes are found.

On careful examination of the stomach, intestines, liver, biliary appendages, spleen, kidney, ureters, bladder, prostate, pancreas and adrenal glands, no changes are found other than those recorded in the anatomic diagnosis.

There is a nodule beneath the pleura in the eighth interspace just to the left of the vertebral column which is 2 cm. long and 0.8 cm. wide and is adherent to the intercostal nerve in that space. There is a second large, irregular nodular mass made up of a number of smaller nodules, which lies in the hollow of the sacrum just posterior to the rectum. This mass is half the size of the fist and is not adherent to the sacrum. It is adherent to the serosa of the rectum, but has not penetrated the muscular walls of the lower gut. There are no other nodules visible in the inner walls of the trunk cavities.

The brain weighs approximately 1,400 gm. There is a moderate edema of the pia over the vertex and over the temporal lobes. The pia is everywhere smooth and glistening and is not thickened. There is a firm, fibrous tumor in the left middle fossa, the size of a small walnut, which is intimately connected with the gasserian ganglion.

There is a similar tumor in each cerebellopontine angle, each measuring about 4.1 by 3.5 by 2.1 cm. These tumors have caused depressions in the cerebral and cerebellar hemispheres which come in relation with them.

There is a small nodule 0.4 cm. in diameter connected with the left third nerve. There are numerous nodules varying in size from a split pea to a Lima bean, intimately connected with the roots of the spinal nerves. There is one large tumor 8 cm. long and 2 cm. in diameter in the cauda, which has caused marked pressure on the terminal filaments of the cord.

There are three nodules connected with the left vagus nerve. The smallest is the size of a pea and is at the level of the hyoid bone and the largest is the size of a hazelnut, this being the nodule described just above the left clavicle. The third nodule is Lima bean sized and is adherent to the larger nodule just described.

Aside from their variation in size the tumors in this body do not vary grossly. They are all very firm, cut with resistance and the surfaces so made are of a gray-white color. There are no evidences of softening or degeneration in any of the tumors. Microscopically these tumors also present the same structure. Fibrous tissue predominates and presents a characteristic whorl formation. With Pal-Weigert and other suitable stains persistent nerve fibers are demonstrable in every tumor. They are most numerous in sections of the large tumors of the brain and in the tumors of the posterior roots of the cord. Here nerve fibers are seen running directly into the tumor masses from the ganglia. A study of sections stained by the Bielschowsky method was undertaken to determine if there was any evidence of peripheral regeneration of nerve fibers from proliferated sheath of Schwann cells, such as has been described by Bruce and Dawson.[1] No such evidence was found. The tumors in the case reported by them, however, consisted almost entirely of nerve fibers and in this respect differed from our case, in which the tumors consist for the most part of fibrous tissue.

In the fifth cervical segment of the cord is a wedge-shaped tumor connected with the posterior horn but originating in posterior roots, which has apparently pushed itself into the cord substance so that its presence was not suspected until the cord was sectioned. Notwithstanding some distortion of the cord due to the presence of the tumor, there is no degeneration of the long fiber tracts at this or other levels. Histologically this tumor does not differ from tumors of other parts of the nervous system. The posterior root fibers of this horn are merely pushed to one side by the tumor mass and they present no evidence of degeneration. Nearly all of the posterior roots of the cord are the site of tumors and in many segments the anterior roots are also involved.

Sections of the cortex taken from the right motor region demonstrate microscopically a rather extensive

1. Multiple Neuromata of the Central Nervous System; Their Structure and Histogenesis, Rev. Neurol. and Psychiat., 1913, xi, Nos. 3, 4, 5 and 6.

proliferation of connective tissue about the vessels and lymphatics. There has been considerable hyaline degeneration of this new-formed tissue.

Scattered diffusely through the cortex and white matter of the motor, frontal and temporal regions are small groups of cells which have no resemblance to ganglion cells or to any of the types of cells found in a normal brain. They are large, polymorphous, vesiculated, contain many fine dark granules and the nuclei are small, dense and lie at one side of the cell. They are devoid of processes. They occur in groups or heaps, in our case fifty to one hundred cells being present in each heap, and resemble those seen in tuberous sclerosis, a condition which is found most frequently in the brains of idiots and of imbecile epileptics. It has been reported in connection with von Recklinghausen's disease in approximately ten instances, but since it must be searched for microscopically, it has probably been frequently missed.

About one of the pial vessels is a calcified plaque which is of especial interest because there are no evidences of calcification elsewhere in the body. This plaque completely surrounds an artery and is 2 mm. in diameter.

May 10, 1915.

TWO CASES OF ATRESIA ANI ET RECTI WITH PSEUDOHERMAPHRODITISMUS FEMININUS EXTERNUS

O. J. PEDERSON

(From the Pathological Laboratory, Northwestern University Medical School, Chicago)

The cases presented in this paper are two full-term fetuses with almost identical malformations. These consist of absence of anus and rectum; external genitalia of male type; internal genitalia of female type; persistence of the cloaca; non-union of the two halves of the uterus; imperforate urethra.

Only a few such cases are found in literature. These have been reported by Ahlfeld, Cruveilhier, Rose, Wagstaffe, Müller, Kuliga, and Koch.

In Case 1, the overdistended large intestine terminates in the posterior wall of a thin-walled sac interposed between it and the bladder, and is continued downward to the bladder as a fibrous ridge through which a fine probe may be passed indicating a communication between bladder and intestine. On each lateral wall of the thin-walled sac which is probably the vagina is situated a horn of the ununited uterus. Each horn has a tube and an ovary. The ureters open into the blodder. The external genitalia are male like, but urethral opening is absent. There is no anal orifice.

In Case 2, the large intestine terminates on the dorsal wall of the distended cloaca, which is the only hollow organ in the pelvis. On each side of the gut lies a horn of the ununited uterus posterolaterally on the wall of the cloaca. Each horn has a tube and an ovary. The uteri do not open into the cloaca. The ureter seems to terminate in the wall of the horn but on dissection is found to open into a separate chamber which communicates with the cloaca by a fine aperture. Between these ureteral apertures is found the narrow passage communicating with the terminal end of the large gut. The external genitalia are of male type, but the urethra is closed. No trace of anus.

The anatomic diagnosis in these cases is: (1) Atresia ani et recti et communicatio recti cum vesica urinaria; (2) pseudohermaphroditismus femininus externus cum atresia urethrae; (3) uterus duplex separatus cum vagina simplice (Case 1) et vagina duplice separata, (Case 2).

The etiology of this condition is as yet on a theoretical basis. Ahlfeld explains it as due to overdistention of the cloaca following delay in the formation of the openings. Kuliga ascribes it to persistence of the omphalomesenteric artery and absence of the hypogastric arteries. But in these two cases the hypogastric arteries are present. Koch speaks of a spontaneous arrest of development, and the probability of some mechanical influences affecting the process in the first month.

From a review of embryology, I come to the conclusion that from whatever origin, overgrowth of mesoderm is the single cause for this complex type of anomaly. In the sixth week before the union of the Müllerian ducts and before the rupture of the urogenital and anal membranes the mesoderm spread beyond its limits and prevented the formation of these openings. Then resulted distention of the cloaca, with incomplete division and with failure of the urogenital ridges to unite. The second result was overgrowth of the external genitalia, notably in the region of the pars pelvina of the urogenital sinus. Thus were formed the elongated penis-like structure and the unpaired scrotal area, which later became raised up to form the scrotal sac.

May 10, 1915.

SYSTEMIC AND LOCAL INFECTIONS IN RELATION TO IRIDOCYCLITIS

ERNEST E. IRONS

AND

E. V. L. BROWN

There were fifty-four cases of lesions of the uveal tract included in the series. Forty-four of these occurred in persons suffering from a single infection, or if more than one infection was present, a careful weighing of all available data indicated that one infection was clearly more active, and in all probability the one related etiologically to the disease of the eye.

Summarizing the probable cause in these forty-four cases, syphilis appears in fourteen, alone in five cases, associated with other infections in nine; gonococcal infection in ten, seven times alone, and three times with other infections; tuberculosis in eleven, nine times alone, and twice with other infections; suppurative processes in the teeth, tonsils, sinuses, or genito-urinary organs in nine; in five of these but one infection was present, in four there were other possible sources of infection. The latter group (teeth, ton-

sils, sinuses, genito-urinary) includes cases which without special investigation would be classed as of "rheumatic" iritis. It is probable that in routine examinations in an eye clinic certain of the gonococcal cases would also appear in this "rheumatic" group.

Of the remaining ten cases of the series, nine presented problems of diagnosis, not due to difficulty of finding an adequate cause, but of picking out which one of several coincident infections was responsible for the trouble in the eye. In all nine syphilis was present, and probably was the cause of the iritis in several. Active gonococcal infection was present in six; tuberculosis in five; extensive dental infection in three; and tonsillar infection in three. Stated in another way, in the nine cases there were twenty-six "adequate" causes. To particularize: in each of two of the nine there were two infectious processes, each "adequate"; in four there were three infections; in two there were four infections, and in one there were five infections. This last patient suffered from an active syphilis, gonococcal infection, tuberculosis, had badly infected tonsils, and alveolar abscesses. Eight of the nine cases of this group were dispensary patients. Although the difficulties of classification of cases with multiple infection is much greater among dispensary than among private patients, yet careful search revealed more than one active infectious process in five of twenty-three private patients.

It might be inferred from the above that overenthusiasm led us to include slight grades of inflammation, processes which under ordinary circumstances would hardly be dignified as foci of infection. But infections have not been included unless they were to a large extent closed processes, or of such a character as are well recognized as capable of giving rise to other metastatic lesions (joints, or skin, etc.). In explanation of the multiplicity of infections in dispensary cases it should be remarked that poor food and surroundings, careless habits of life, and often the physical handicap of the one or two infections previously acquired, undoubtedly facilitate the devel-

opment of new infections. Moreover, the unfavorable effect of one infection on a host may make him more susceptible to other infections, which would not gain headway in a normal person.

May 10, 1915.

OBSERVATIONS ON THE PROTEOLYTIC ENZYMES OF BACILLUS PROTEUS

A. I. KENDALL
AND
A. W. WALKER

A study of the soluble (exo-) proteolytic enzyme of *Bacillus proteus* has led to the following conclusions regarding its formation and activity:

1. The proteolytic enzyme of *Bacillus proteus* appears in an active state in filtrates of plain broth and plain gelatin cultures of the organism.

2. The enzyme is not present in an active state in dextrose broth or dextrose gelatin cultures.

3. Very small amounts of dextrose (up to 0.3 per cent.) added to plain broth or plain gelatin delay the appearance of enzyme.

4. Large percentages of dextrose prevent its formation.

5. The enzyme, freed from bacteria by filtration through sterile porcelain filters, will liquefy dextrose gelatin as readily as plain, dextrose-free gelatin.

6. The liquefaction of plain or dextrose gelatin by the bacteria-free enzyme is not accompanied by the liberation of ammonia—deaminization is independent of the action of enzyme per se.

7. The proteolytic enzyme is a preparatory enzyme in the sense that it prepares protein for assimilation by the organism; it has no demonstrable rôle in the intracellular utilization of the protein by the organism itself.

8. The enzyme does not appear in an active state in media containing utilizable sugars; it appears only

when protein or protein derivatives are being utilized for energy.

9. The observations presented above do not preclude the possibility of conditions other than those obtaining in the experiments recorded, exercising some influence on the formation of this enzyme.

May 10, 1915.

THE PREPARATION OF COLLOIDAL EMULSIONS OF CHOLESTEROL

KAETHE DEWEY

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In nearly all the experimental work on cholesterol, this substance has been given by mouth, either as food which is rich in cholesterol, such as beef brain and yolks of eggs, or as the pure product dissolved in some fat or oil, generally in sunflower oil. Where feeding was continued over long periods, rather large quantities of such solvents were used, in some cases as much as a kilogram. The infiltration which follows the ingestion of appreciable amounts of such fats is considered by those who have investigated it not to be a pathological one. It is questionable, however, whether it is entirely negligible when the immediate action of cholesterol on the tissues is to be studied. At any rate, it was desirable to avoid an oily solvent in my work, since I wished to produce a direct hypercholesterolemia by intravenous and intraperitoneal injections. A watery colloid emulsion of cholesterol, a method for the preparation of which is given by Porges and Neubauer,[1] had been employed by me[2] in a previous experimental study of cholesterol and found to be satisfactory. Instead of Merck's pure cholesterol, I used a preparation obtained from gallstones. These were pulverized and the cholesterol extracted with ether by the Soxhlet apparatus. For

1. Porges and Neubauer: Physikalisch chemische Untersuchungen über das Lecithin und Cholesterin, Biochem. Ztschr., 1907, vii, 152.

2. Dewey, Kaethe: The Effect of Cholesterol on Phagocytosis, Jour. Infect. Dis., 1914, xv, 472.

the separation of all saponifiable substances from this ether extract, a method was employed which is based largely on Kumagawa and Suto.[3] Five gm. of the dried ether extract are dissolved in 350 to 400 c.c. of petroleum ether; to this, 70 c.c. of a 1 per cent. absolute alcoholic solution of KOH and 30 c.c. of distilled water are added, thus making a 70 per cent alcoholic solution. The mixture is shaken and the ether solution of cholesterol separated from the alcoholic solution of soaps in the separating funnel. The petroleum ether is evaporated and the dry cholesterol treated in the same manner a second and, if necessary, a third time. It is finally recrystallized with alcohol. The melting point of this substance was between 146 and 147 F.

In order to make a watery colloidal emulsion from this crystalline substance by the method of Porges and Neubauer, cholesterol is dissolved in acetone and added in small amounts to large quantities of distilled water, while stirring it. The acetone is evaporated and another portion of the acetone solution is added, the acetone evaporated, and so on, until all the cholesterol necessary for the desired strength has been used. The emulsion is finally filtered through an asbestos filter. When large quantities of this preparation and of a rather high concentration are needed, this method is not an ideal one; it consumes an enormous amount of time. Attempts at adequate modifications seemed therefore indicated. The chief difficulty, not rarely encountered, was in getting all of the cholesterol into the state of a fine emulsion; some of it frequently floated on top as "foam." The observation, however, that this so-called foam when taken up with fresh acetone will easily and quickly go into the emulsion, whether or not acetone is still present, led to the modification of the method. To a concentrated solution of cholesterol in acetone, warm distilled water is added slowly until the acetone solution when heated does not turn clear again. Enough acetone is added to remove the precipitate. The clear

3. Kumagawa and Suto: Bestimmung des Cholesterins nebst den anderen unverseifbaren Substanzen, Biochem. Ztschr., 1908, viii, 315.

solution is then slowly poured into warm distilled water. If some of the cholesterol foams out, it is taken up with acetone and added to the emulsion. It is then boiled in small quantities and filtered through an ordinary filter, using a fresh one for every new portion. The total is reduced to the desired strength by vacuum distillation and the emulsion finally filtered again.

The making of such an emulsion still takes considerable time, but, once made, it is an exceedingly satisfactory preparation. It is very stable. Such emulsions have been kept for three months and longer without undergoing any apparent changes. Heat does not affect them; they can be sterilized in the autoclave repeatedly. They were tested by adding serum and fresh blood from normal and cholesterolized rabbits as well as physiological salt solution. By none of these fluids was the cholesterol precipitated out from its emulsion state. Whatever the ultimate fate of the colloid cholesterol in the blood, it is evidently carried off by the blood stream from the place of the injection without leaving any deposits there. It was thus possible, for example, to make thirty injections in daily succession into the veins of the ears of one rabbit. After intraperitoneal injections, cholesterol deposits in small nodules were generally found on the mesentery, liver, spleen and the under surface of the diaphragm.

Twelve rabbits were injected with such colloid emulsions, the injections varying as to the amount and concentration of the emulsion and the periodicity and length of time during which they were continued. The effects on various tissues such as the liver, spleen, adrenal, aorta, bone marrow and chiefly the kidneys, with quantitative estimation of the cholesterol content of the blood, bile and urine, in most of the cases, will be reported in another paper. I may only mention that in one rabbit gallstones of various sizes were produced, which filled almost the entire gall bladder. In three other rabbits, numerous "sandy concretions" were found in the bile.

May 10, 1915.

CARCINOMA OF THE LOWER THIRD OF THE ESOPHAGUS WITH COMPLETE OCCLUSION OF THE LUMEN BY A SILVER DIME

JOHN W. NUZUM

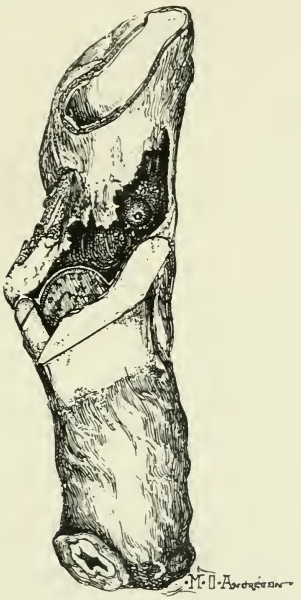
(From the Pathological Laboratory of Cook County Hospital, Chicago)

J. A., a colored barber 57 years of age, entered the Cook County Hospital March 25, 1915, to the service of Dr. Grinker, with distinctive signs of tabes dorsalis. He was extremely emaciated and weak and said he had been unable to take solid food for a year previous because of nausea and vomiting about one-half hour after eating. He had never noticed any blood in the vomitus. He had suffered constantly with dull aching pain in the epigastrium and for the two weeks previous to admission liquids even were vomited immediately after taking. He was an old colored man too feeble to take much interest in his surroundings, with a cachexia, but no signs of any neoplasm. A diagnosis of carcinoma of the stomach was made. Death occurred after five days.

Anatomic Diagnosis.—Circular carcinoma (?) of the lower third of the esophagus; moderate diminution in the lumen of the cardiac end of the esophagus; marked emaciation; corroded silver dime in the lower third of the esophagus; pressure necrosis of the esophageal walls at the site of the foreign body; nodular (syphilitic) and senile sclerosis of the thoracic and abdominal aorta; narrow persistent membranous eustachian valve; fatty changes in the myocardium, liver and kidneys; cloudy swelling of the kidneys and liver; moderate edema of the cerebral cortex; senile cataract of the left eye; missing teeth. The following brief description is taken from the original record of the necropsy:

"The walls of the lowermost 11 cm. of the esophagus are diffusely thickened by a dense white connective tissue infiltration. The lumen of the cardiac

orifice is markedly constricted, diameter only 0.5 cm. Eight cm. above the cardiac orifice a corroded silver dime is obliquely situated, completely occluding the lumen, and here the esophageal walls are 1 cm. thick. Above the dime there is a sacular dilatation. Microscopic examination of the thick wall proves it to



Illustrating the location of a corroded silver dime which caused complete occlusion of the lumen of the esophagus. Note the very marked diminution of the lumen at the cardiac orifice—it admits only a very fine probe.

be an epithelioma with many so-called 'epithelial pearls' scattered throughout the various sections and it was subsequently learned that the patient swallowed the coin one week previous to admission."

May 10, 1915.

DUODENOJEJUNAL HERNIA

JOHN W. NUZUM

If the great omentum together with the transverse colon are deflected upward and backward over the thorax, by making gentle traction on the jejunum at the site of the duodenojejunal junction, a delicate band may be seen passing upward and backward to fix the flexure to the posterior parietal peritoneum; this band is the suspensory ligament of Treitz. Just behind the band lies the superior duodenojejunal fossa with its apex looking upward toward the pancreas, its mouth downward toward a second pouch, the inferior duodenojejunal pouch of Treitz. Herniation of the small bowel may take place into either one of these fossae and a hernia of this class I wish briefly to describe.[1]

F. S., a photo finisher, aged 42, entered the Hospital of the House of Correction, April 17, 1915, and died one week later, it was thought from delirium tremens The necropsy was made by Dr. E. R. LeCount, who found "on the left side in the angle formed by the transverse and descending colon and projecting forward and to the right a little, but downward chiefly, a sac 11 cm. long by 10 cm. wide, and 7 cm. thick. The width is transversely directed and the length forward, downward, and to the right. There is gas or air in this at present and the front wall is so thin that coils of the small bowel are easily seen shining through it. It fills about one fifth of the entire opening made into the abdomen. The opening into the sac on the right side admits two finger tips snugly. The small bowel enters here and the loop of small bowel that lies in front and visible is the distal end of that in the sac; that entering lies behind and is seen when the small bowel is thrown up over the thorax. The bowel moves easily through this opening and there are no signs of obstruction anywhere. The transverse colon above the sac is not adherent to it,

1. For the author's report of a similar hernia see Two Unusual Internal Hernias, Tr. Chicago Path. Soc., 1914, ix, 191.

but the omentum is. In order to ascertain the relation of the sac to the splenic flexure the sternum is removed and it is seen that the upper end of the hernial sac extends in front of the pancreas and up behind the greater fundus of the stomach. Below, the sigmoid is in contact with the sac, but is not adherent to it. The bowel that enters the sac is that part all proximal to the distal 123.5 cm. of the small bowel measuring up from the ileocecal valve."

On examination after removal from the body, the sac is found to be roughly the shape of a large kidney and the hilus corresponds both in shape and relative position to the orifice of the hernial sac. The walls are composed of peritoneum, very thin, glistening and transparent, through which the distended loops of the small bowel can be easily seen. It is 20 cm. in its vertical dimension, 12 cm. transversely, and 7 cm. wide, and weighs 630 gm.

The orifice of the sac is 6 to 8 cm. in diameter; when stretched, 8 to 10 cm. The right side of the opening is formed by the root of the mesentery of the small bowel, the left side by the mesentery of the descending colon, the floor by the "mesentericomesocolic" fold. The inferior mesenteric vein together with the left colic artery course upward, parallel to each other, along the mouth of the sac in the left wall to reach its upper margin, where the vein arches over the opening toward the right side of the body. The sac contains the proximal half of the small bowel, readily reduced through the opening. There is no sign of recent or old strangulation.

These conditions compare in all respects to left duodenojejunal hernia. Among the chief features with which it corresponds to this variety of internal hernia is the location of the inferior mesenteric vein and left colic artery, both within the fold of the sac in its left wall. Approximately seventy similar cases have been recorded, in only ten with the hernia causing death. Once the condition was diagnosed correctly before operation; in another the bowel was reduced through the mouth of the sac and the hernial cavity packed with sterile cotton. The patient made

an uneventful recovery dying later of typhoid fever, confirmed by necropsy.

The hernia described here was in no way concerned in causing death, which was from nodular hyperplastic syphilitic leptomeningitis, with a gumma of the hypophysis cerebri, and bilateral hypostatic bronchopneumonia.

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